

strictly prohibited.

FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/BPN
15 L1
102210 BPN/RL
L4 0 L1/BPN
(L1 (L) BPN/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION
FULL ESTIMATED COST 2.26
7.57

FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/IMF
15 L1
390491 IMF/RL
L5 0 L1/IMF
(L1 (L) IMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY

SESSION
FULL ESTIMATED COST 9.83 2.26

FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PEP
15 L1
1687596 PEP/RL
L6 1 L1/PEP
(L1 (L) PEP/RL)

=> DIS L6 1 CBIB ABS HITRN

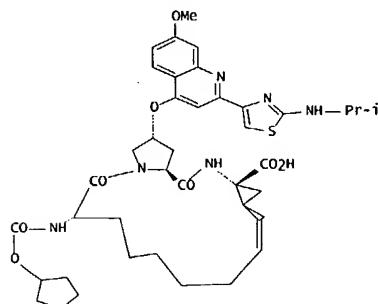
L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2004:310970 Document No. 140:327091 Potent inhibitor of HCV serine protease.

Chen, Shirlyn; Nehmiz, Gerhard; Croenlein, Jens Oliver;
Steinmann,
Gerhard; Gunn, Jocelyn Abella; Costa, Phuong Do (Boehringer Ingelheim

International G.m.b.H., Germany). PCT Int. Appl. WO 2004030670

A1: 20040415, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,
BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,
EC, EE,
EG, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
BY, KG,

KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES,
FI, FR,
GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG,
TR.
(English). CODEN: PIXXD2. APPLICATION: WO 2003-US30402
20030925.
PRIORITY: US 2002-PV414940 20020930; US 2002-PV421904 20021029;
US 2002-PV433834 20021216; US 2003-PV443662 20030130.
GI



I

AB Disclosed are oral pharmaceutical compns., kits and methods of treating and preventing Hepatitis C Viral (HCV) infections wherein Compound (I), a potent inhibitor of HCV serine protease, or a pharmaceutically acceptable salt thereof, is administered in a selected dosage range. Also disclosed are the use of I or a pharmaceutically acceptable salt thereof, as a control substance for validating an HCV replication assay and also as a control substance for determining the relative effectiveness of one or more substances, alone or in combination, to inhibit the replication of HCV.

IT 300832-84-2
RL: PAC (Pharmacological activity); PEP (Physical, engineering
or chemical process); PYP (Physical process); THU (Therapeutic
use); BIOL (Biological study); PROC (Process); USES (Uses)
(potent inhibitor of HCV serine protease)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY

SESSION
FULL ESTIMATED COST 14.95 5.12

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL ENTRY

SESSION
CA SUBSCRIBER PRICE 0.70 -0.70 -

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FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PUR
15 L1
201134 PUR/RL
L7 0 L1/PUR
(L1 (L) PUR/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY

SESSION
FULL ESTIMATED COST 17.21 2.26

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL ENTRY
SESSION

CA SUBSCRIBER PRICE
0.70

0.00

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S (L1/SPN OR L1/CPN)
15 L1
1660968 SPN/RL
6 L1/SPN
(L1 (L) SPN/RL)
15 L1
1155 CPN/RL
0 L1/CPN
(L1 (L) CPN/RL).
L8 6 (L1/SPN OR L1/CPN)

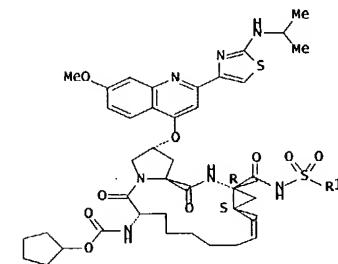
=> FOCUS L8
PROCESSING COMPLETED FOR L8
L9 6 FOCUS L8 1-

=> DIS L9 1- CBIB ABS HITRN
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):Y

L9 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:580783 Document No. 141:261053 Synthesis of BILN 2061, an HCV
NS3 Protease Inhibitor with Proven Antiviral Effect in Humans.
Faucher,
Anne-Marie; Bailey, Murray D.; Beaulieu, Pierre L.; Brochu,
Christian;
Duceppe, Jean-Simon; Ferland, Jean-Marie; Ghiro, Elise; Gorys,
Vida;
Halmos, Ted; Kawai, Stephen H.; Poirier, Martin; Simoneau,
Bruno;
Tsantrizos, Youla S.; Llinas-Brunet, Montse (Chemistry

MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU,
SC, SD,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU,
ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG,
CH, CI,
CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR,
NE, NL,
PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
APPLICATION: WO
2003-CA1604 20031020. PRIORITY: US 2002-PV421414 20021025; US
2002-PV433820 20021216; US 2003-PV442768 20030127.

GI

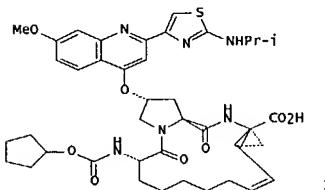


AB Macrocyclic peptides I [R1 is (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, aryl or heteroaryl] or their pharmaceutically-acceptable salts were prepared as inhibitors of the hepatitis C virus (HCV) NS3 protease. Thus, I (R = Me) was prepared by a multistep sequence involving peptide coupling, olefin metathesis to form the macrocycle and methanesulfonamidation.

IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:168624 Document No. 140:350045 Structure-activity study on a novel series of macrocyclic inhibitors of the hepatitis C virus NS3 protease leading to the discovery of BILN 2061. Llinas-Brunet, Montse; Bailey,

Department:
Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.).
Organic
Letters, 6(17), 2901-2904 (English) 2004. CODEN: ORLEF7. ISSN: 1523-7060. Publisher: American Chemical Society.
GI



AB The synthesis of BILN 2061 (I), a hepatitis C virus (HCV) NS3 protease inhibitor with proven antiviral effect in humans, was accomplished in a convergent manner from four building blocks. The procedure described here was suitable for the preparation of multigram quantities of BILN 2061 for preclin. pharmacol. evaluation.

IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyl macrocycle BILN-2061, an HCV NS3 protease inhibitor with proven antiviral effect in humans)

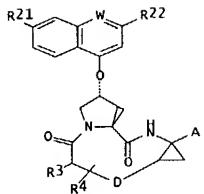
L9 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:370958 Document No. 140:357673 Preparation of macrocyclic peptides active against the hepatitis C virus. Llinas-Brunet, Montse; Bailey, Murray D. (Boehringer Ingelheim International G.m.b.h., Germany). PCT Int. Appl. WO 2004037855 A1 20040506, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,

Murray D.; Bolger, Gordon; Brochu, Christian; Faucher, Anne-Marie; Ferland, Jean Marie; Garneau, Michel; Ghiro, Elise; Gorys, Vida; Grand-Maitre, Chantal; Halmos, Ted; Lapeyre-Paquette, Nicole; Liard, Francine; Poirier, Martin; Rheaume, Manon; Tsantrizos, Youla S.; Lamarre, Daniel (Departments of Chemistry and Biological Sciences, Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.). Journal of Medicinal Chemistry, 47(7), 1605-1608 (English) 2004. CODEN: JMCMAR.

ISSN: 0022-2623. Publisher: American Chemical Society.
AB From the discovery of competitive hexapeptide inhibitors, potent and selective HCV NS3 protease macrocyclic inhibitors have been identified. Structure-activity relationship studies were performed focusing on optimizing the N-terminal carbamate and the aromatic substituent on the (4R)-hydroxyproline moiety. Inhibitors meeting the potency criteria in the cell-based assay and with improved oral bioavailability in rats were identified. BILN 2061 was selected as the best compound, the first NS3 protease inhibitor reported with antiviral activity in man.

IT 300832-84-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(BILN 2061; structure-activity study on a novel series of macrocyclic inhibitors of the hepatitis C virus NS3 protease leading to the discovery of BILN 2061)

L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:648255 Document No. 139:197768 Preparation of macrocyclic peptides active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy; Llinas-Brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.), U.S. US 6608027 B1 20030819, 90 pp., Cont.-in-part of U.S. Ser. No. 542,675, abandoned. (English). CODEN: USXXAM. APPLICATION: US 2001-760946 20010116. PRIORITY: US 1999-PV128011 19990406; US 2000-542675 20000403.
GI



I

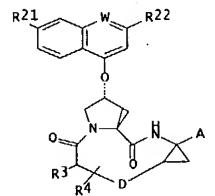
AB Macrocyclic peptides I [$W = CH$ or N ; $R21 = H$, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; $R22 = H$, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; $R3 =$ hydroxy, NH_2 , aryl- or heteroarylamino, $NHCOR32$, $CONHR32$, $C02R32$, where $R32$ is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; $R4 = H$ or from one to three substituents at any carbon atom of chain D ; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [$W = N$; $R21$, $R22$, $R4 = H$; $A = CO2H$; $R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E$ (syn to acid)] was prepared and showed $IC50 > 0.1 \mu M$ in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(uses) (preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS ON STN
2003:511084 Document No. 139:69527 Preparation of macrocyclic compounds as inhibitors of hepatitis C virus. Campbell, Jeffrey Allen; Good, Andrew Charles (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003053349 A2 20030703, 225 pp. DESIGNATED STATES: $W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,$

TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW:
AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN:
PIXXD2. APPLICATION: WO 2000-CA353 20000403. PRIORITY: US
1999-PV128011
19990406.
GI



I

AB Macrocyclic peptides I [$W = CH$ or N ; $R21 = H$, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; $R22 = H$, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; $R3 =$ hydroxy, NH_2 , aryl- or heteroarylamino, $NHCOR32$, $CONHR32$, $C02R32$, where $R32$ is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; $R4 = H$ or from one to three substituents at any carbon atom of chain D ; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [$W = N$; $R21$, $R22$, $R4 = H$; $A = CO2H$; $R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E$ (syn to acid)] was prepared and showed $IC50 > 0.1 \mu M$ in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIIXD2. APPLICATION: WO 2002-US39926 20021213. PRIORITY: US 2001-PV344080 20011220; US 2002-PV382103 20020520. GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to macrocyclic compds. I [$R1 =$ (cyclo)alkyl; $R2 = H$, halo, alkyl, alkoxy, cycloalkoxy, (un)substituted aryl or heterocycl; $R3 = H$, halo, CF₃, alkoxy, cycloalkoxy; $R4 = NH_2$ or $NHR6$, where $R6$ is alkanoyl, alkylaminocarbonyl, or carbalkoxy; Q is a 3-9 atom (un)saturated alkylene chain optionally containing 1-3 heteroatoms O, S, SO, or SO₂], including methods for their synthesis and use in pharmaceutical compns. for therapeutic or prophylactic prevention or treatment of hepatitis C virus (HCV) infection. Thus, 3,13-diazatricyclo[11.3.0.0_{4,6}]hexadec-7-ene derivative II was prepared by a multistep procedure and assayed for inhibition of HCV NS3/4A protease ($IC50 < 5 \mu M$).

IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic compds. as inhibitors of hepatitis C virus)

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS ON STN
2000:725652 Document No. 133:296659 Preparation of macrocyclic peptides active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy; Linas-brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). PCT Int. Appl. WO 2000059929 A1 20001012, 154 pp. DESIGNATED STATES: $W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,$

(uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

=> FILE REGISTRY
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION
FULL ESTIMATED COST 25.57
42.78
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL ENTRY
SESSION
CA SUBSCRIBER PRICE -4.20
4.90

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STRUCTURE FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6
DICTIONARY FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registrys.htm>

=> d his

(FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCII, BIOPARTNERS, BIOPARTNERS, BIOPARTNERS, BIOTECHNO, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPB, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON 26 OCT 2004

L1 FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
 1 S 300832-84-2/RN
 SET SMA OFF
 DEL SEL Y
 SEL RN
 SET SMA LOGIN
 INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
 SEA F1 AND OPTICAL?/FA

L2 QUE 300832-84-2/B1 AND OPTICAL?/FA

L3 FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
 0 S L1/BMF

L4 FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
 0 S L1/BPN

L5 FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
 0 S L1/IMF

L6 FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
 1 S L1/PEP

L7 FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
 0 S L1/PUR

L8 FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
 6 S (L1/SPN OR L1/CPN)

L9 FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
 6 FOCUS L8 1-

FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

=> file hcplus
 COST IN U.S. DOLLARS SINCE FILE
 TOTAL ENTRY
 SESSION FULL ESTIMATED COST 0.84
 43.62
 43.62
 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
 TOTAL ENTRY
 SESSION CA SUBSCRIBER PRICE 0.00
 4.90

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
 FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 11
 L10 15 L1
 => l10 and crystal
 1117482 CRYSTAL
 6001001 CRYSTALS
 1385437 CRYSTAL
 (CRYSTAL OR CRYSTALS)
 L11 0 L10 AND CRYSTAL
 => l10 and crystal?
 1605797 CRYSTAL?
 L12 0 L10 AND CRYSTAL?
 => l10 and alcohol
 217243 ALCOHOL
 149677 ALCOHOLS
 339514 ALCOHOL
 (ALCOHOL OR ALCOHOLS)
 L13 0 L10 AND ALCOHOL
 => l10 and pd<20030327
 23271868 PD<20030327
 (PD<20030327)
 L14 3 L10 AND PD<20030327
 => d 114 1-3 ibib
 L14 ANSWER 1 OF 3 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2004:252197 HCPLUS Full-text
 DOCUMENT NUMBER: 140:281350
 TITLE: Spiro compounds for inhibiting the first-pass effect
 INVENTOR(S): Harris, James W.
 PATENT ASSIGNEE(S): Bioavailability System, LLC, USA
 SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S.
 Ser. No. 793,416.
 DOCUMENT TYPE: CODEN: USXXCO
 Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

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| US 2004058982 | A1 | 20040325 | US 2003-422848 |
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| US 6248776 | B1 | 20010619 | US 1999-251467 |
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| US 6476066 | B1 | 20021105 | US 2001-793416 |
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| | | | US 2001-793416 A2 |
| 20010227 | | | US 1997-56382P P |
| 19970826 | | | US 1997-997259 A2 |
| 19971223 | | | |
| OTHER SOURCE(S): MARPAT | | | 140:281350 |

L14 ANSWER 2 OF 3 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:886572 HCPLUS Full-text
 DOCUMENT NUMBER: 140:122161
 TITLE: An NS3 protease inhibitor with antiviral effects in humans infected with hepatitis C virus
 AUTHOR(S): Lamarre, Daniel; Anderson, Paul C.; Bailey, Murray; Pierre; Mireille; Goudreau, Lagace, Poupart, E.; St. Gerhard; Weldon, Steven
 CORPORATE SOURCE: Boehringer Ingelheim (Canada) Ltd, Laval, QC, H7S 2G5, Nature (London, United Kingdom) (2003), 426(6963), 186-189
 SOURCE: CODEN: NATUAS; ISSN: 0028-0836
 PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES
 AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 3 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:725652 HCPLUS Full-text
 DOCUMENT NUMBER: 133:296659
 TITLE: Preparation of macrocyclic peptides active against the hepatitis C virus
 INVENTOR(S): Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Nathalie; Halmos, Teddy; Llinas-brunet, Montse Boehringer Ingelheim (Canada) Ltd., Can.
 PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 154 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
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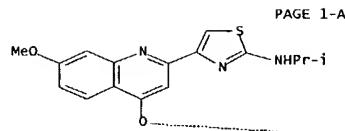
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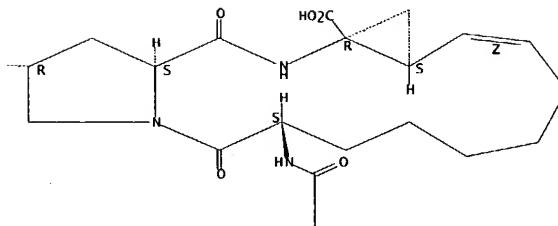
L14 ANSWER 1 OF 3 HCPLUS COPYRIGHT 2004 ACS ON STN
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 (spiro compds. for inhibiting the first-pass effect)
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 (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



PAGE 1-A

PAGE 1-B



PAGE 2-B



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      F2      22 SCISEARCH
      F3      18 BIOSIS
      F4      15 INVESTEXT
      F5      13 MEDLINE
      F6      11 PCTFULL
      F7      10 CAPLUS
      F8      10 DDFU
      F9      10 DRUGU
      F10     8 BIOTECHNO
      F11     6 USPATFULL
      F12     4 LIFESCI
      F13     4 PASCAL
      F14     4 TOXCENTER
      F15     3 ESBIOBASE
      F16     3 IMSDRUGNEWS
      F17     3 NLDB
      F18     2 ADISCTI
      F19     2 BIOENG
      F20     2 CBNB
      F21     2 COMPENDEX
      F22     2 PHIN
      F23     2 WPIDS
      F24     2 WPINDEX
      F25     1 BABS
      F26     1 CIN
      F27     1 EMBAL
      F28     1 IFIPAT
      F29     1 PROMT

```

=> index f1-f29
 COST IN U.S. DOLLARS
 TOTAL
 SESSION
 FULL ESTIMATED COST 1.14
 94.22
 94.22
 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
 TOTAL ENTRY
 SESSION SINCE FILE
 CA SUBSCRIBER PRICE 0.00 -
 4.90
 4.90
 INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTTEXT, MEDLINE, PCTFULL,
 CAPLUS, DDFU,
 DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
 ESBIOBASE,
 IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
 WPIDS,
 WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20
 ON 26 OCT 2004
 29 FILES IN THE FILE LIST IN STNINDEX
 Enter SET DETAIL ON to see search term postings or to view
 search error messages that display as 0* with SET DETAIL OFF.
 => d his 114-
 (FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004)
 L14 3 L10 AND PD<20030327
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 ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
 BABS,
 BIBLIODATA, BIOPARTNERS, BIOMARKERS, BIOENGINEERING, BIOENG, BIOSIS,
 BIOTECHARS,
 BIOTECHDS, BIOTECHNO, BLldb, CABA, CANCERLIT, ...' ENTERED AT
 15:24:55 ON 26 OCT 2004
 SEA BILN 2061

 2 FILE ADISCTI
 1 FILE BABS
 2 FILE BIOENG
 18 FILE BIOSIS
 8 FILE BIOTECHNO
 10 FILE CAPLUS
 2 FILE CBNB
 1 FILE CIN
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 3 FILE ESBIOBASE
 1 FILE IFIPAT
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 15 FILE INVESTTEXT
 4 FILE LIFESCI
 13 FILE MEDLINE
 3 FILE NLDB
 4 FILE PASCAL
 11 FILE PCTFULL
 2 FILE PHIN
 1 FILE PROMT
 22 FILE SCISEARCH
 4 FILE TOXCENTER
 6 FILE USPATFULL
 2 FILE WPIDS
 2 FILE WPINDEX
 L15 QUE BILN 2061

 INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTTEXT, MEDLINE, PCTFULL,
 CAPLUS,
 DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
 ESBIOBASE,
 IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
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F2      6 USPATFULL
F3      4 EMBASE
F4      3 SCISEARCH
F5      3 BIOTECHNO

=> file f3-5,f1,f2
COST IN U.S. DOLLARS          SINCE FILE
TOTAL                           ENTRY

SESSION
FULL ESTIMATED COST          1.71
95.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL                           ENTRY

SESSION
CA SUBSCRIBER PRICE          0.00
4.90

FILE 'EMBASE' ENTERED AT 15:27:48 ON 26 OCT 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 15:27:48 ON 26 OCT 2004
Copyright (c) 2004 The Thomson Corporation.

FILE 'BIOTECHNO' ENTERED AT 15:27:48 ON 26 OCT 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights
reserved.

FILE 'PCTFULL' ENTERED AT 15:27:48 ON 26 OCT 2004
COPYRIGHT (C) 2004 Univetio

FILE 'USPATFULL' ENTERED AT 15:27:48 ON 26 OCT 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> l16, dup rem
L17      0 L16, DUP REM

```

```

=> l16
L18      25 L16

=> dup rem
ENTER L# LIST OR (END):l18
PROCESSING COMPLETED FOR L18
L19      21 DUP REM L18 (4 DUPLICATES REMOVED)

=> l19 and pd<20030327
  1 FILES SEARCHED...
  3 FILES SEARCHED...
L20      2 L19 AND PD<20030327

=> d l20 1-2 ibib hitstr abs kwic
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

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The following are valid formats:

The default display format is BIB.

```

ABS ----- AB
ALL ----- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL, AB,
CT, RN, CN, NP, CO, GEN
BIB ----- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL
CBIB ----- Compressed bibliographic data
DALL ----- ALL, delimited for post-processing
IABS ----- ABS, with a text label
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- CT, RN, CN, NP, CO, GEN
TRIAL ----- TI, CT, RN, CN, NP, CO, GEN
(SAM, TRI)
HIT ----- All fields containing hit terms
HITIND ----- IND
KWIC ----- All hit terms plus 20 words on either side
OCC ----- List of display fields containing hit terms
and number of occurrences in each field

```

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields, enter the display field codes. For a list of display field codes, enter 'HELP DFIELDS' at an arrow prompt (>). Examples of formats include: 'BIB'; 'AB'; 'SO,ST'. You may specify the format fields in any order, and the information will be displayed in the same order as the format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be used with the DISPLAY ACC command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):iall

L20 ANSWER 1 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003468113 EMBASE Full-text
 TITLE: Current therapy and new molecular approaches to
 antiviral treatment and prevention of hepatitis C.
 AUTHOR: Hugle T.; Cerny A.
 CORPORATE SOURCE: Dr. A. Cerny, Clinica Medica, Ospedale Civico,
 CH-6903 Lugano, Switzerland. andreas.cerny@bluewin.ch
 SOURCE: Reviews in Medical Virology, (2003) 13/6
 (361-371).
 Refs: 79
 ISSN: 1052-9276 CODEN: RMVIEW
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 004 Microbiology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 039 Pharmacy
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ABSTRACT: Current therapeutic options for hepatitis C are limited, especially for genotype 1. For genotypes 2 and 3, pegylated interferon in combination with ribavirin, can lead to a sustained virological response in up to 80% of patients. Unfortunately, adverse effects of IFN and ribavirin are a major problem and the list of contraindications for HCV therapy is long, including decompensated cirrhosis of the liver and psychiatric disorders. Therefore, alternative therapeutic approaches are needed. New delivery options for IFN and ribavirin are aimed at optimising efficiency and reducing adverse effects. Recent progress in the molecular virology of HCV has identified new targets for antiviral intervention. Inhibition of HCV gene expression and replication as well as immunotherapeutic concepts aimed at enhancing the cellular immune response against HCV are being explored. Solution of the crystal structures of HCV key enzymes led to the design of specific inhibitors including compounds active against the well characterised NS3 serine protease and RNA-dependent RNA polymerase which are currently in the early phase. Clinical investigation. New strategies for inhibiting HCV gene expression include the use of antisense oligodeoxynucleotides and ribozymes. Immunomodulation by agents such as inosine monophosphate dehydrogenase inhibitors, thymosin-alpha 1, histamine or amantadine are being

studied in combination with IFN and/or ribavirin. Immunotherapeutic vaccination with recombinant HCV E1 protein improved host immunity against HCV and thus seems to be a promising new option. Copyright © 2003 John Wiley & Sons, Ltd.

CONTROLLED TERM:

Medical Descriptors:
 *hepatitis C: DT, drug therapy
 *hepatitis C: ET, etiology
 *hepatitis C: PC, prevention
 *infection prevention
 virus gene
 genotype
 drug response
 drug contraindication
 drug delivery system
 side effect: SI, side effect
 gene expression
 drug targeting
 immunotherapy
 enzyme structure
 crystal structure
 drug design
 drug activity
 antiviral activity
 protein targeting
 immunomodulation
 vaccination
 Hepatitis C virus
 immune response
 cellular immunity
 hemolytic anemia: SI, side effect
 mental disease: SI, side effect
 flu like syndrome: SI, side effect
 leukopenia: SI, side effect
 thrombocytopenia: SI, side effect
 teratogenicity
 virus replication
 drug hypersensitivity: SI, side effect
 rash: SI, side effect
 human
 nonhuman
 clinical trial
 review
Drug Descriptors:
 alpha interferon: AE, adverse drug reaction
 alpha interferon: CT, clinical trial
 alpha interferon: CB, drug combination
 alpha interferon: DT, drug therapy
 alpha interferon: TO, drug toxicity
 alpha interferon: PR, pharmaceutics
 alpha interferon: PD, pharmacology
 alpha interferon: SC, subcutaneous drug
 ribavirin: AE, adverse drug reaction

administration

ribavirin: CT, clinical trial
 ribavirin: CB, drug combination
 ribavirin: CM, drug comparison
 ribavirin: DT, drug therapy
 ribavirin: PK, pharmacokinetics
 ribavirin: PD, pharmacology
 ribavirin: PO, oral drug administration
 albumin conjugate: PR, pharmaceutics
 liposome: PR, pharmaceutics
 polyaminoacid: PR, pharmaceutics
 polyaminoacid: PO, oral drug administration
 ribavirin derivative: AE, adverse drug reaction
 ribavirin derivative: CT, clinical trial
 ribavirin derivative: CB, drug combination
 ribavirin derivative: CM, drug comparison
 ribavirin derivative: DT, drug therapy
 ribavirin derivative: PD, pharmacology
 viramidine: AE, adverse drug reaction
 viramidine: CT, clinical trial
 viramidine: CB, drug combination
 viramidine: CM, drug comparison
 viramidine: DT, drug therapy
 viramidine: PD, pharmacology
 levovirin: AE, adverse drug reaction
 levovirin: CT, clinical trial
 levovirin: CM, drug comparison
 levovirin: DT, drug therapy
 levovirin: PD, pharmacology
 proteinase inhibitor: AE, adverse drug reaction
 proteinase inhibitor: CT, clinical trial
 proteinase inhibitor: DO, drug dose
 proteinase inhibitor: DT, drug therapy
 proteinase inhibitor: PK, pharmacokinetics
 proteinase inhibitor: PD, pharmacology
 proteinase inhibitor: PO, oral drug
 biln 2061: AE, adverse drug reaction
 biln 2061: CT, clinical trial
 biln 2061: DO, drug dose
 biln 2061: DT, drug therapy
 biln 2061: PK, pharmacokinetics
 biln 2061: PD, pharmacology
 biln 2061: PO, oral drug administration
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 vx 950: PD, pharmacology
 virus protein
 protein NS5B
 RNA directed DNA polymerase inhibitor: CT,
 RNA directed DNA polymerase inhibitor: DT, drug
 RNA directed DNA polymerase inhibitor: PD,
 jtk 003: CT, clinical trial
 jtk 003: DT, drug therapy
 jtk 003: PD, pharmacology
 ribozyme: AE, adverse drug reaction

trial

ribozyme: CT, clinical trial
 ribozyme: DT, drug therapy
 ribozyme: TO, drug toxicity
 ribozyme: PD, pharmacology
 hepatozyme: AE, adverse drug reaction
 hepatozyme: CT, clinical trial
 hepatozyme: DT, drug therapy
 hepatozyme: TO, drug toxicity
 hepatozyme: PD, pharmacology
 antisense oligodeoxynucleotide: CT, clinical
 antisense oligodeoxynucleotide: DT, drug therapy
 antisense oligodeoxynucleotide: PD, pharmacology
 isis 14803: CT, clinical trial
 isis 14803: DT, drug therapy
 isis 14803: PD, pharmacology
 RNA derivative: DV, drug development
 RNA derivative: DT, drug therapy
 RNA derivative: PD, pharmacology
 small interfering rna: DV, drug development
 small interfering rna: DT, drug therapy
 small interfering rna: PD, pharmacology
 monoclonal antibody: DT, drug therapy
 monoclonal antibody: PD, pharmacology
 xtl 002: DT, drug therapy
 xtl 002: PD, pharmacology
 cicavir: DT, drug therapy
 cicavir: PD, pharmacology
 immunomodulating agent: CB, drug combination
 immunomodulating agent: DT, drug therapy
 thymosin alpha1: CT, clinical trial
 thymosin alpha1: CB, drug combination
 thymosin alpha1: DO, drug dose
 thymosin alpha1: DT, drug therapy
 thymosin alpha1: PD, pharmacology
 inosinate dehydrogenase inhibitor: CB, drug
 inosinate dehydrogenase inhibitor: DT, drug
 inosinate dehydrogenase inhibitor: PD,

combination therapy pharmacology

merimepodib: CT, clinical trial
 merimepodib: CB, drug combination
 merimepodib: DT, drug therapy
 merimepodib: PD, pharmacology
 unindexed drug
 unclassified drug
 CAS REGISTRY NO.: 37205-61-1;
 198821-22-6,
 CHEMICAL NAME: (ribavirin) 36791-04-5; (proteinase inhibitor)
 (thymosin alpha1) 69521-94-4; (merimepodib)
 198821-38-4
 (1) Vx 950; (2) Jtk 003; Biln 2061; Isis 14803;
 Xtl 002
 COMPANY NAME: (1) Vertex; (2) Akros; Ribozyne Pharmaceuticals;
 Sciclone; RegeneRx; Maxim

administration

clinical trial
 therapy
 pharmacology

L20 ANSWER 2 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN
 ACCESSION NUMBER: 2003195244 EMBASE Full-text
 TITLE: Hepatitis C virus therapies: Current treatments,
 targets and future perspectives.
 AUTHOR: Walker M.P.; Appleby T.C.; Zhong W.; Lau J.Y.N.;
 CORPORATE SOURCE: Z. Hong, Ribapharm Inc., Hyland Avenue, Costa
 Mesa, CA,
 SOURCE:
 United States. zhihong@ribapharm.com
 Antiviral Chemistry and Chemotherapy, (2003) 14/1
 (1-21).
 Refs: 208
 ISSN: 0956-3202 CODEN: ACCHEH
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT:
 004 Microbiology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ABSTRACT:
 Chronic hepatitis C virus (HCV) infection is the cause of an emerging global epidemic of chronic liver disease. Current combination therapies are at best 80% efficacious and are often poorly tolerated. Strategies to improve the therapeutic response include the development of novel interferons, nucleoside analogues with reduced haemolysis compared with ribavirin and inosine 5'-monophosphate dehydrogenase inhibitors. Compounds in preclinical or early clinical trials include small molecules that inhibit virus-specific enzymes (such as the serine proteases, RNA polymerase and helicase) or interfere with translation (including antisense molecules, siRNA and ribozymes). Advances in understanding HCV replication, obtaining a sub-genomic replicon and contriving potential small animal models, in addition to solving crystallographic structures for the replication enzymes, have improved prospects for developing novel therapies. This review summarizes current and evolving treatments for chronic hepatitis C infection. In addition, progress in HCV targets and drug discovery tools valuable in the search for novel anti-HCV agents is detailed.

| | | |
|------------------|---|---|
| CONTROLLED TERM: | <p>Medical Descriptors: *hepatitis C: DT, drug therapy *hepatitis C: EP, epidemiology *hepatitis C: ET, etiology *chronic liver disease: ET, etiology drug efficacy drug tolerance hemolytic anemia: SI, side effect side_effect: SI, side effect alanine aminotransferase blood level virus replication replicon crystal structure RNA translation untranslated region internal ribosome entry site monotherapy virus load treatment outcome treatment indication immunomodulation drug safety treatment failure chimpanzee transgenic mouse Hepatitis GB virus B IC 50 structure activity relation drug structure virus assembly human nonhuman clinical trial review priority journal Drug Descriptors: *antivirus agent: AE, adverse drug reaction *antivirus agent: CT, clinical trial *antivirus agent: AN, drug analysis *antivirus agent: CB, drug combination *antivirus agent: CM, drug comparison *antivirus agent: DV, drug development *antivirus agent: DO, drug dose *antivirus agent: DT, drug therapy *antivirus agent: PD, pharmacology *antivirus agent: IV, intravenous drug *antivirus agent: SC, subcutaneous drug alpha interferon: AE, adverse drug reaction alpha interferon: CB, drug combination alpha interferon: CM, drug comparison alpha interferon: DO, drug dose alpha interferon: DT, drug therapy alpha interferon: PD, pharmacology nucleoside derivative: AN, drug analysis nucleoside derivative: CM, drug comparison</p> | nucleoside derivative: DV, drug development nucleoside derivative: PR, pharmaceutics nucleoside derivative: PD, pharmacology ribavirin: AE, adverse drug reaction ribavirin: CT, clinical trial ribavirin: CB, drug combination ribavirin: CM, drug comparison ribavirin: DO, drug dose ribavirin: DT, drug therapy ribavirin: PD, pharmacology inosinate dehydrogenase inhibitor: CM, drug inosinate dehydrogenase inhibitor: DT, drug inosinate dehydrogenase inhibitor: PD, serine proteinase: EC, endogenous compound RNA polymerase: EC, endogenous compound helicase: EC, endogenous compound ribozyme: EC, endogenous compound recombinant alpha2a interferon: CM, drug recombinant alpha2a interferon: DO, drug dose recombinant alpha2a interferon: DT, drug therapy recombinant alpha2a interferon: PD, pharmacology recombinant alpha2a interferon: SC, subcutaneous administration recombinant alpha2b interferon: CM, drug recombinant alpha2b interferon: DO, drug dose recombinant alpha2b interferon: DT, drug therapy recombinant alpha2b interferon: PD, pharmacology recombinant alpha2b interferon: SC, subcutaneous administration consensus interferon: CM, drug comparison consensus interferon: DO, drug dose consensus interferon: DT, drug therapy consensus interferon: PD, pharmacology consensus interferon: SC, subcutaneous drug peginterferon alpha2b: CT, clinical trial peginterferon alpha2b: CB, drug combination peginterferon alpha2b: CM, drug comparison peginterferon alpha2b: DO, drug dose peginterferon alpha2b: DT, drug therapy peginterferon alpha2b: PD, pharmacology peginterferon alpha2a: CT, clinical trial peginterferon alpha2a: CB, drug combination peginterferon alpha2a: CM, drug comparison peginterferon alpha2a: DO, drug dose peginterferon alpha2a: DT, drug therapy peginterferon alpha2a: PD, pharmacology levovirin: CT, clinical trial levovirin: AN, drug analysis levovirin: CM, drug comparison |
| administration | | |
| administration | | |
| administration | <p>levovirin: DV, drug development levovirin: DO, drug dose levovirin: DT, drug therapy levovirin: PD, pharmacology viramidine: CT, clinical trial viramidine: AN, drug analysis viramidine: CM, drug comparison Viramidine: DV, drug development viramidine: DO, drug dose viramidine: DT, drug therapy viramidine: PD, pharmacology merimepodib: CT, clinical trial merimepodib: AN, drug analysis merimepodib: CB, drug combination merimepodib: CM, drug comparison merimepodib: DV, drug development merimepodib: DT, drug therapy merimepodib: PD, pharmacology thymosin alpha1: CT, clinical trial thymosin alpha1: AN, drug analysis thymosin alpha1: CB, drug combination thymosin alpha1: DV, drug development thymosin alpha1: DO, drug dose thymosin alpha1: DT, drug therapy thymosin alpha1: PD, pharmacology thymosin alpha1: SC, subcutaneous drug</p> | administration biln 2061: CT, clinical trial biln 2061: DO, drug dose biln 2061: PD, pharmacology biln 2061: PO, oral drug administration peptide derivative: AN, drug analysis peptide derivative: DV, drug development peptide derivative: PD, pharmacology peptide alpha keto acid: AN, drug analysis peptide alpha keto acid: DV, drug development peptide alpha keto acid: PD, pharmacology pyrrolidine derivative: AN, drug analysis pyrrolidine derivative: DV, drug development pyrrolidine derivative: PD, pharmacology pyrrolidine 5,5 lactam: AN, drug analysis pyrrolidine 5,5 lactam: DV, drug development pyrrolidine 5,5 lactam: PD, pharmacology IDdb3: DV, drug development IDdb3: PD, pharmacology unindexed drug unclassified drug isis 14803 gw 3112 gw 2549 gw 0569 n [4 [[6,7 dihydro 2 (4 methylphenyl) 5h 8 yl]carbonyl]amino]benzyl] n,n dimethyl 2h |
| administration | <p>amantadine: CT, clinical trial amantadine: AN, drug analysis amantadine: CB, drug combination amantadine: CM, drug comparison amantadine: DV, drug development amantadine: PD, pharmacology recombinant interleukin 12: CT, clinical trial recombinant interleukin 12: AN, drug analysis recombinant interleukin 12: CB, drug combination recombinant interleukin 12: CM, drug comparison recombinant interleukin 12: DV, drug development recombinant interleukin 12: DO, drug dose recombinant interleukin 12: DT, drug therapy recombinant interleukin 12: PD, pharmacology histamine: CT, clinical trial histamine: AN, drug analysis histamine: CB, drug combination histamine: DV, drug development histamine: DT, drug therapy histamine: PD, pharmacology gamma interferon: CT, clinical trial gamma interferon: AN, drug analysis gamma interferon: CB, drug combination gamma interferon: DV, drug development gamma interferon: DT, drug therapy gamma interferon: PD, pharmacology proteinase inhibitor: CT, clinical trial proteinase inhibitor: DO, drug dose proteinase inhibitor: PD, pharmacology proteinase inhibitor: PO, oral drug</p> | administration benzocyclohepten tetrahydropyran CAS REGISTRY NO.: 37259-58-8; 6; (peginterferon 198153-51-4; alpha1) (histamine) [4 [[6,7 tetrahydropyran 4 CHEMICAL NAME: 779; Amd biln 2061: PO, oral drug administration peptide derivative: AN, drug analysis peptide derivative: DV, drug development peptide derivative: PD, pharmacology peptide alpha keto acid: AN, drug analysis peptide alpha keto acid: DV, drug development peptide alpha keto acid: PD, pharmacology pyrrolidine derivative: AN, drug analysis pyrrolidine derivative: DV, drug development pyrrolidine derivative: PD, pharmacology pyrrolidine 5,5 lactam: AN, drug analysis pyrrolidine 5,5 lactam: DV, drug development pyrrolidine 5,5 lactam: PD, pharmacology IDdb3: DV, drug development IDdb3: PD, pharmacology unindexed drug unclassified drug isis 14803 gw 3112 gw 2549 gw 0569 n [4 [[6,7 dihydro 2 (4 methylphenyl) 5h 8 yl]carbonyl]amino]benzyl] n,n dimethyl 2h 4 aminium chloride 1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane) (ribavirin) 36791-04-5; (serine proteinase) (RNA polymerase) 9014-24-8; (helicase) 42613-29- (recombinant alpha2b interferon) 98530-12-2; (alpha2b) 215647-85-1; (peginterferon alpha2a) (merimepodib) 198821-22-6, 198821-38-4; (thymosin 69521-94-4; (amantadine) 665-66-7, 768-94-5; 51-45-6, 56-92-8, 93443-21-1; (gamma interferon) 82115-62-6; (proteinase inhibitor) 37205-61-1; (n dihydro 2 (4 methylphenyl) 5h benzocyclohepten 8 yl]carbonyl]amino]benzyl] n,n dimethyl 2h aminium chloride 229005-80-5; (1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane)) 155148-31-5 (1) Vx 497; (2) Ceplene; (3) Biln 2061; (4) Isis 14803; Zadaxin; Gw 3112; Gw 2549; Gw 0569; Tak 3100; IDdb3 |

COMPANY NAME: (1) Vertex (United States); (2) Maxim; (3)
 Boehringer Ingelheim; (4) Isis (United States); Ribapharm;
 Merck (United States); Glaxo SmithKline (United
 Kingdom); Bristol Myers Squibb (United States); Celera (United
 States); viropharma; Japanese tobacco; IRBM

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(FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
 AQUALINE, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
 BIOTECHIDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
 CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
 26 OCT 2004

FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004

L1 1 S 300832-84-2/RN
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INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
 SEA E1 AND OPTICAL?/FA

L2 QUE 300832-84-2/BI AND OPTICAL?/FA

FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
 0 S L1/BMF

FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
 0 S L1/BPN

FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
 0 S L1/IMF

FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
 1 S L1/PEP

FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
 0 S L1/PUR

FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
 6 S (L1/SPN OR L1/CPN)

L9 6 FOCUS L8 1-

FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
 WPIDS, WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT, SCISEARCH
 26 OCT ENTERED AT 15:26:20 ON
 2004

SEA L15 AND CRYSTAL?

4 FILE EMBASE
 3 FILE SCISEARCH
 9 FILE PCTFULL
 3 FILE BIOTECHNO
 6 FILE USPATFULL

L16 QUE L15 AND CRYSTAL?

FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
 AT 15:27:48 ON 26 OCT 2004
 L17 0 L16, DUP REM
 L18 25 L16
 L19 21 DUP REM L18 (4 DUPLICATES REMOVED)
 L20 2 L19 AND PD-20030327

=> stnindex

ENTER FILE OR CLUSTER NAMES (NONE):all
 FILE 'ENCOMPLIT' ACCESS NOT AUTHORIZED
 FILE 'ENCOMPLIT2' ACCESS NOT AUTHORIZED
 FILE 'ENCOMPPAT' ACCESS NOT AUTHORIZED
 FILE 'ENCOMPPAT2' ACCESS NOT AUTHORIZED
 COST IN U.S. DOLLARS

TOTAL SINCE FILE ENTRY

SESSION FULL ESTIMATED COST 16.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY

TOTAL 0.00

INDEX 'IMOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
 AGRICOLA, ALUMINUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
 BABS, BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
 BIOTECHABS,
 BIOTECHIDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...'
 ENTERED AT 15:32:46 ON 26 OCT 2004

143 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
 search error messages that display as 0* with SET DETAIL OFF.

FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004

L10 15 S L1
 L11 0 L10 AND CRYSTAL
 L12 0 L10 AND CRYSTAL?
 L13 0 L10 AND ALCOHOL
 L14 3 L10 AND PD-20030327

FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

INDEX 'IMOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
 AGRICOLA, ALUMINUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
 BABS, BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
 BIOTECHABS,
 BIOTECHIDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
 15:24:55 ON 26 OCT 2004

SEA BILN 2061

 2 FILE ADISCTI
 1 FILE BABS
 2 FILE BIOENG
 18 FILE BIOSIS
 8 FILE BIOTECHNO
 10 FILE CAPLUS
 2 FILE CBNB
 1 FILE CIN
 2 FILE COMPENDEX
 10 FILE DDFU
 10 FILE DRUGU
 1 FILE EMBAL
 42 FILE EMBASE
 3 FILE ESBIOBASE
 1 FILE IFIPAT
 3 FILE IMSDRUGNEWS
 15 FILE INVESTTEXT
 4 FILE LIFESCI
 13 FILE MEDLINE
 3 FILE NLDB
 4 FILE PASCAL
 11 FILE PCTFULL
 2 FILE PHIN
 1 FILE PROMT
 22 FILE SCISEARCH
 4 FILE TOXCENTER
 6 FILE USPATFULL
 2 FILE WPIDS
 2 FILE WPINDEX

L15 QUE BILN 2061

INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTTEXT, MEDLINE, PCTFULL,
 CAPLUS,
 DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
 ESBIOBASE,

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 FILE '2MOBILITY'
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 FILE 'BIOTECHIDS'
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=> ciluprevir/
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For a list of field codes for the current file, enter "HELP SFIELDS"
at an arrow prompt (>).

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L21 QUE CILUPREVIR
=> d rank
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F2      2 ESBIOBASE
F3      2 MEDLINE
F4      2 SCISEARCH
F5      1 DDFU
F6      1 DRUGU

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=> fil f1-6
COST IN U.S. DOLLARS          SINCE FILE
TOTAL                           ENTRY
SESSION
FULL ESTIMATED COST          5.70
118.15
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL                           ENTRY
SESSION
CA SUBSCRIBER PRICE          0.00
4.90
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FILE 'MEDLINE' ENTERED AT 15:39:01 ON 26 OCT 2004

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FILE 'SCISSEARCH' ENTERED AT 15:39:01 ON 26 OCT 2004
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FILE 'DDFU' ACCESS NOT AUTHORIZED

FILE 'DRUGU' ENTERED AT 15:39:01 ON 26 OCT 2004
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=> s 121
L22 10 L21

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1 FILES SEARCHED...
2 FILES SEARCHED...
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'20030327' NOT A VALID FIELD CODE
L23 1 L22 AND PD<20030327

=> d 123

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On STN
AN 2004039472 EMBASE Full-text
TI Gateways to Clinical Trials.
AU Bayes M.; Rabasseda X.; Prous J.R.
CS M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain
mbayes@prous.com
SO Methods and Findings in Experimental and Clinical Pharmacology,
(2003) 25/10 (831-855).
Refs: 145
ISSN: 0379-0355 CODEN: MFPDX
CY Spain
DT Journal: General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION 8.37
FULL ESTIMATED COST
126.52
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 22, 2004 (20041022/UP).

=> 123 all
MISSING OPERATOR L23 ALL
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.
=> d 123 all
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE' - CONTINUE? (Y)/N:y

L23 ANSWER 1 OF 1 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN
AN 2004039472 EMBASE Full-text
TI Gateways to Clinical Trials.
AU Bayes M.; Rabasseda X.; Prous J.R.
CS M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain
mbayes@prous.com
SO Methods and Findings in Experimental and Clinical Pharmacology,
(2003) 25/10 (831-855).
Refs: 145
ISSN: 0379-0355 CODEN: MFPDX
CY Spain
DT Journal: General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity®, the drug discovery and development portal, <http://integrity.prous.com>. This issue focuses on the following selection of drugs: Abetimus sodium, adalimumab, alefacept, alemtuzumab, almotriptan, AMGN-007, anakinra, anti-CTLA-4 Mab, L-arginine hydrochloride, arzoxifene hydrochloride, astemizole, atazanavir sulfate, atizumab; Belimumab, BG-9928, binodenoson, bosentan, botulinum toxin type B, bovine lactoferrin, BufferGel; Caspofungin acetate, ciclesonide, cilomilast, ciluprevir, clofarabine, CVT-3146; Darbepoetin alfa, desloratadine, diflomotecan, doripenem, dronedarone hydrochloride, drotrecogin alfa (activated), DT388-GM-CSF, duloxetine hydrochloride, E-5564, efalizumab, enfuvirtide, esomeprazole magnesium, estradiol acetate, ETC-642,

exenatide, exisulind, ezetimibe; Febuxostat; Gallium maltolato, ganirelix acetate, garenoxacin mesilate, gefitinib; H11, HuMax; IL-15, ID-1, TGFIV-C, imatinib mesylate, ISIS-14803, ITF-1697, ivabradine hydrochloride; KRN-5500; L-365260, levetiracetam, levosimendan, licofeline, linezolid, LJP-1082, lopinavir, lumiracoxib; MCC-478, melatonin, morphine hydrochloride, morphine-6-glucuronide, moxidectin; N-Acetylcarnosine, natalizumab, NM-702, NNC-05-1869, NSC-703940; Octahapton OM-89, natalizumab, omeprazole/sodium bicarbonate, OPC-28326, ospemifene; PEG-filgrastim peginterferon alfa-2a, pegsunercept, piperfenidone, pralmorelin, pregabalin; Recombinant glucagon-like peptide-1 (7-36) amide, repifermin, RSD-1235; S-8184, selodenoson, sodium dichloroacetate, suberanilohydroxamic acid; TAS-102, terfenadine, teriparatide, tipranavir troxacitabine; Ximelagatran; YM-337. ©COPYRG. 2003 Prous Science. All rights reserved.

CT Medical-Descriptors:
*drug monitoring
drug indication
drug efficacy
drug safety
side effect: SI, side effect
patient compliance
drug tolerability
liver toxicity: SI, side effect
bleeding: SI, side effect
disease exacerbation
systemic lupus erythematosus: SI, side effect
digestive system ulcer: SI, side effect
neutropenia: SI, side effect
teratogenicity: SI, side effect
human
clinical trial
review
Drug Descriptors:
abetimus: CT, clinical trial
abetimus: IV, intravenous drug administration
adalimumab: AE, adverse drug reaction
adalimumab: CT, clinical trial
linezolid: CT, clinical trial
alemtuzumab: CT, clinical trial
ivabradine: CT, clinical trial
ivabradine: IV, intravenous drug administration
recombinant interleukin 1 receptor blocking agent: CT, clinical trial
recombinant interleukin 1 receptor blocking agent: IA,
intraarterial drug administration
glucagon like peptide 1: CT, clinical trial
glucagon like peptide 1: SC, subcutaneous drug administration
astemizole: CT, clinical trial
atazanavir: CT, clinical trial
bosentan: CT, clinical trial
botulinum toxin B: CT, clinical trial
caspofungin: CT, clinical trial
ciclesonide: CT, clinical trial
cilmilast: CT, clinical trial

falizumab: CT, clinical trial
imatitinib: CT, clinical trial
terfenadine: CT, clinical trial
tipranavir: CT, clinical trial
tipranavir: PO, oral drug administration
ximelagatran: CT, clinical trial
ximelagatran: PO, oral drug administration
ym 337: CT, clinical trial
moxidectin: CT, clinical trial
estradiol: CT, clinical trial
novel erythropoiesis stimulating protein: CT, clinical trial
novel erythropoiesis stimulating protein: IV, intravenous drug administration
novel erythropoiesis stimulating protein: SC, subcutaneous drug administration
desloratadine: CT, clinical trial
desloratadine: PO, oral drug administration
diflomotecan: CT, clinical trial
diflomotecan: IV, intravenous drug administration
diflomotecan: PO, oral drug administration
morphine: CT, clinical trial
etiracetam: CT, clinical trial
doripenem: CT, clinical trial
duloxetine: CT, clinical trial
unindexed drug
RN (abetimus) 167362-48-3, 169147-32-4; (adalimumab) 331731-18-1;
(linezolid) 165800-03-3; (alemtuzumab) 216503-57-0; (ivabradine) 148849-67-
6, 148870-80-8, 155974-00-8; (glucagon like peptide 1) 89750-14-1;
(astemizole) 68844-77-9; (atazanavir) 198904-31-3; (bosentan)
147536-97-8, 157212-55-0; (caspofungin) 189768-38-5; (ciclesonide) 126544-47-
6; (cilmilast) 153259-65-5; (efalizumab) 214745-43-4; (imatinib)
152459-95-5, 220127-57-1; (terfenadine) 50679-08-8; (tipranavir)
174484-41-4; (ximelagatran) 192939-46-1, 260790-58-7;
(moxidectin) 113507-06-5; (estradiol) 50-28-2; (desloratadine) 100643-71-8;
(diflomotecan) 220997-97-7; (morphine) 52-26-6, 57-27-2;
(etiracetam) 102767-28-2, 33996-58-6; (doripenem) 148016-81-3; (duloxetine)
116539-59-4, 136434-34-9
CN Ym 337

=> DIS HIST

(FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)
INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
AQUASCI, BIOPARTNERS, BIOPARTNERS, BIOPARTNERS, BIOPARTNERS,
BIOTECHNOLOGY,
BIOTECHNOLOGY, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
CROPB, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON

26 OCT 2004

L1 FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
1 S 300832-84-2/RN
SET SMA OFF
DEL SEL Y
SEL RN
SET SMA LOGIN
INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
SEA E1 AND OPTICAL?/FA
L2 QUE 300832-84-2/BI AND OPTICAL?/FA

FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
0 S L1/BMF
FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
0 S L1/BPN
FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
0 S L1/IMF
FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
1 S L1/PEP
FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
0 S L1/PUR
FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
6 S (L1/SPN OR L1/CPN)
L9 6 FOCUS L8 1-

FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004

L10 15 S L1
L11 0 L10 AND CRYSTAL
L12 0 L10 AND CRYSTAL?
L13 0 L10 AND ALCOHOL
L14 3 L10 AND PD<20030327

FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

INDEX 'IMOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
26 OCT 2004

SEA BILN 2061

2 FILE ADISCTI

INDEX 'IMOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:32:46 ON
26 OCT 2004

SEA CILUPREVIR/CN

0* FILE IMOBILITY
0* FILE 2MOBILITY
0* FILE ADISCTI
0* FILE AEROSPACE
0* FILE ALUMINIUM
0* FILE ANTE
0* FILE APOLLIT
0* FILE AQUALINE
0* FILE AQUASCI
0* FILE BABS
0* FILE BIBLIODATA
0* FILE BIOCOMMERCE
0* FILE BIOENG
SEA CILUPREVIR/

0* FILE IMOBILITY
SEA CILUPREVIR

1 FILE DDFU
1 FILE DRUGU
3 FILE EMBASE
2 FILE ESBIOBASE
2 FILE MEDLINE
2 FILE SCISEARCH

L21 QUE CILUPREVIR

FILE 'EMBASE, ESBIOBASE, MEDLINE, SCISEARCH, DRUGU' ENTERED AT
15:39:01
ON 26 OCT 2004
L22 10 S L21
L23 1 L22 AND PD<20030327

FILE 'STNGUIDE' ENTERED AT 15:40:30 ON 26 OCT 2004

FILE 'EMBASE' ENTERED AT 15:41:46 ON 26 OCT 2004

FILE 'STNGUIDE' ENTERED AT 15:41:46 ON 26 OCT 2004

=>

---Logging off of STN---

1 FILE BABS
2 FILE BIOENG
18 FILE BIOSIS
8 FILE BIOTECHNO
10 FILE CAPLUS
2 FILE CBNB
1 FILE CIN
2 FILE COMPENDEX
10 FILE DDFU
10 FILE DRUGU
1 FILE EMBAL
42 FILE EMBASE
3 FILE ESBIOBASE
1 FILE IFIPAT
3 FILE IMSDRUGNEWS
15 FILE INVESTTEXT
4 FILE LIFESCI
13 FILE MEDLINE
3 FILE NLDB
4 FILE PASCAL
11 FILE PCTFULL
2 FILE PHIN
1 FILE PROMT
22 FILE SCISEARCH
4 FILE TOXCENTER
6 FILE USPATFULL
2 FILE WPIDS
2 FILE WPINDEX
L15 QUE BILN 2061

INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTTEXT, MEDLINE, PCTFULL,
CAPLUS,
DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
2004
SEA L15 AND CRYSTAL?

4 FILE EMBASE
3 FILE SCISEARCH
9 FILE PCTFULL
3 FILE BIOTECHNO
6 FILE USPATFULL
L16 QUE L15 AND CRYSTAL?

FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
AT
15:27:48 ON 26 OCT 2004
L17 0 L16, DUP REM
L18 25 L16
L19 21 DUP REM L18 (4 DUPLICATES REMOVED)
L20 2 L19 AND PD<20030327

=>
Executing the logoff script...

=> LOG Y
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION
FULL ESTIMATED COST 0.12
130.58
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL ENTRY
SESSION
CA SUBSCRIBER PRICE 0.00
4.90
STN INTERNATIONAL LOGOFF AT 15:42:43 ON 26 OCT 2004

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1653adk

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

***** Welcome to STN International *****

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NEWS 3 Jul 12 BEILSTEIN enhanced with new display and select options,
NEWS 4 AUG 02 resulting in a closer connection to BABS
IFIPAT/IFIUDB/IFICDB reloaded with new search and display
NEWS 5 AUG 02 fields
Caplus and CA patent records enhanced with European and Japan
NEWS 6 AUG 02 Patent Office Classifications
The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 7 AUG 27 BIOMMERCE: Changes and enhancements to content coverage
NEWS 8 AUG 27 BIOTECHABS/BIOTECHDS: Two new display fields added for legal
NEWS 9 SEP 01 status data from INPADOC
available INPADOC: New family current-awareness alert (SDT)
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NEWS 11 SEP 01 STN Express with Discover!
WPINDEX/WPIINDEX/WPIX New display format, HITSTR, available in
NEWS 12 SEP 27 STANDARDS will no longer be available on STN
NEWS 13 SEP 27 SWETSCAN will no longer be available on STN

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STYL: 'HOME' ENTERED AT 14:34:23 ON 26 OCT 2004

| SESSION | ENTRY |
|---------------------|-------|
| FULL ESTIMATED COST | 0.42 |
| 0.42 | |

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
26 OCT 2004

75 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view search error messages that display as 0* with SET DETAIL OFF.

=> fil reg
COST IN U.S. DOLLARS
TOTAL

SESSION
SINCE FILED
ENTRY

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STRUCTURE FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

SESSION 0.57
FULL ESTIMATED COST
3.05

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/BMF
L3 52155 0 L1/BMF
 (L1 (L) BMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS
TOTAL

SESSION
FULL ESTIMATED COST
F 31

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FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

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=> S L1/BPN
15 L1
102210 BPN/RL
L4 0 L1/BPN
(L1 (L) BPN/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION
FULL ESTIMATED COST 2.26
7.57

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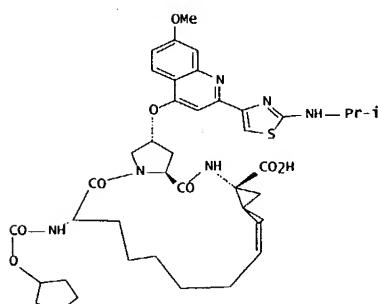
FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/IMF
15 L1
390491 IMF/RL
L5 0 L1/IMF
(L1 (L) IMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY

KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES,
FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG,
TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US30402
20030925. PRIORITY: US 2002-PV414940 20020930; US 2002-PV421904 20021029;
US 2002-PV433834 20021216; US 2003-PV443662 20030130.
GI



AB Disclosed are oral pharmaceutical compns., kits and methods of treating and preventing Hepatitis C Viral (HCV) infections wherein Compound (I), a potent inhibitor of HCV serine protease, or a pharmaceutically acceptable salt thereof, is administered in a selected dosage range. Also disclosed are the use of I or a pharmaceutically acceptable salt thereof, as a control substance for validating an HCV replication assay and also as a control substance for determining the relative effectiveness of one or more substances, alone or in combination, to inhibit the replication of HCV.
300832-84-2

IT RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (potent inhibitor of HCV serine protease)

SESSION
FULL ESTIMATED COST 9.83 2.26

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PEP
15 L1
1687596 PEP/RL
L6 1 L1/PEP
(L1 (L) PEP/RL)

=> DIS L6 1 CBIB ABS HITRN

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS ON STN
2004:310970 Document No. 140:327091 Potent inhibitor of HCV serine protease.
Chen, Shirlynn; Nehmiz, Gerhard; Croenlein, Jens Oliver;
Steinmann, Gerhard; Gunn, Jocelyn Abella; Costa, Phuong Do (Boehringer Ingelheim International G.m.b.H., Germany). PCT Int. Appl. WO 2004030670
A1 20040415, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION
FULL ESTIMATED COST 14.95 5.12
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
TOTAL SINCE FILE
SESSION
CA SUBSCRIBER PRICE 0.70 ENTRY -0.70 -

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PUR
15 L1
201134 PUR/RL
L7 0 L1/PUR
(L1 (L) PUR/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY
SESSION
FULL ESTIMATED COST 17.21 2.26
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
TOTAL SINCE FILE
SESSION
ENTRY

CA SUBSCRIBER PRICE
0.70

0.00

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S (L1/SPN OR L1/CPN)
15 L1
1660968 SPN/RL
6 L1/SPN
(L1 (L) SPN/RL)
15 L1
1155 CPN/RL
0 L1/CPN
(L1 (L) CPN/RL)
L8 6 (L1/SPN OR L1/CPN)

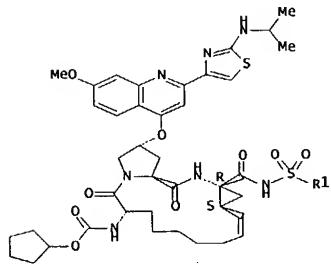
=> FOCUS L8
PROCESSING COMPLETED FOR L8
L9 6 FOCUS L8 1-

=> DIS L9 1- CBIB ABS HITRN
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):Y

L9 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS ON STN
2004:580783 Document No. 140:261053 Synthesis of BILN 2061, an HCV NS3
Protease Inhibitor with Proven Antiviral Effect in Humans.
Faucher,
Anne-Marie; Bailey, Murray D.; Beaulieu, Pierre L.; Brochu,
Christian;
Duceppe, Jean-Simon; Ferland, Jean-Marie; Ghiro, Elise; Gorys,
Vida;
Hajmos, Ted; Kawai, Stephen H.; Poirier, Martin; Tsantrizos,
Bruno;
Tsantrizos, Youla S.; Llinas-Brunet, Montse (Chemistry

MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU,
SC, SD,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU,
ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG,
CH, CI,
CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR,
NE, NL,
PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
APPLICATION: WO
2003-CA1604 20031020. PRIORITY: US 2002-PV421414 20021025; US
2002-PV433820 20021216; US 2003-PV442768 20030127.

GI



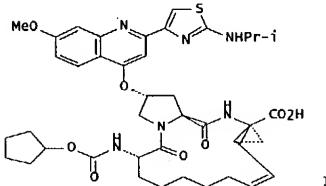
I

AB Macrocyclic peptides I [R1 is (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, aryl or heteroaryl] or their pharmaceutically acceptable salts were prepared as inhibitors of the hepatitis C virus (HCV) NS3 protease. Thus, I (R = Me) was prepared by a multistep sequence involving peptide coupling, olefin metathesis to form the macrocycle and methanesulfonamidation.

IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:168624 Document No. 140:350045 Structure-activity study on a novel series of macrocyclic inhibitors of the hepatitis C virus NS3 protease leading to the discovery of BILN 2061. Llinas-Brunet, Montse; Bailey,

Department,
Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.).
Organic
Letters, 6(17), 2901-2904 (English) 2004. CODEN: ORLEF7. ISSN: 1523-7060. Publisher: American Chemical Society.
GI



AB The synthesis of BILN 2061 (I), a hepatitis C virus (HCV) NS3 protease inhibitor with proven antiviral effect in humans, was accomplished in a convergent manner from four building blocks. The procedure described here was suitable for the preparation of multigram quantities of BILN 2061 for preclin. pharmacol. evaluation.

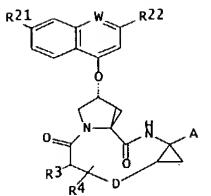
IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyl macrocycle BILN-2061, an HCV NS3 protease inhibitor with proven antiviral effect in humans)

L9 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:370958 Document No. 140:357673 Preparation of macrocyclic peptides active against the hepatitis C virus. Llinas-Brunet, Montse; Bailey, Murray D. (Boehringer Ingelheim International G.m.b.h., Germany). PCT Int. Appl. WO 2004037855 A1 20040506, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,

Murray D.; Bolger, Gordon; Brochu, Christian; Faucher, Anne-Marie; Ferland, Jean Marie; Garneau, Michel; Ghiro, Elise; Gorys, Vida; Grand-Maitre, Chantal; Hajmos, Ted; Lapeyre-Paquette, Nicole; Liard, Francine; Poirier, Martin; Rheaume, Manon; Tsantrizos, Youla S.; Lamarre, Daniel (Departments of Chemistry and Biological Sciences, Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.). Journal of Medicinal Chemistry, 47(7), 1605-1608 (English) 2004. CODEN: JMCMAR.

ISSN: 0022-2623. Publisher: American Chemical Society.
AB From the discovery of competitive hexapeptide inhibitors, potent and selective HCV NS3 protease macrocyclic inhibitors have been identified. Structure-activity relationship studies were performed focusing on optimizing the N-terminal carbamate and the aromatic substituent on the (4R)-hydroxyproline moiety. Inhibitors meeting the potency criteria in the cell-based assay and with improved oral bioavailability in rats were identified. BILN 2061 was selected as the best compound, the first NS3 protease inhibitor reported with antiviral activity in man.
IT 300832-84-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (BILN 2061; structure-activity study on a novel series of macrocyclic inhibitors of the hepatitis C virus NS3 protease leading to the discovery of BILN 2061)

L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:648255 Document No. 139:197768 Preparation of macrocyclic peptides active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Hajmos, Teddy; Llinas-Brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). U.S. US 6608027 B1 20030819, 90 pp., Cont.-in-part of U.S. Ser. No. 542,675 abandoned. (English). CODEN: USXXAM. APPLICATION: US 2001-760946 20010116. PRIORITY: US 1999-PV128011 19990406; US 2000-542675 20000403.
GI



I

MZ, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US39926 20021213. PRIORITY: US 2001-PV344080 20011220; US 2002-PV382103 20020520. GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to macrocyclic compds. I [R1 = (cyclo)alkyl; R2 = H, halo, alkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μ M in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN 2003:511084 Document No. 139:69527 Preparation of macrocyclic compounds as inhibitors of hepatitis C virus. Campbell, Jeffrey Allen; Good, Andrew Charles (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003053349 A2 20030703, 225 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Haimos, Teddy; Linas-brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). PCT Int. Appl. WO 2000059929 A1 20001012, 154 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,

(Uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

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AB Macro cyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μ M in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN 2003:511084 Document No. 139:69527 Preparation of macrocyclic compounds as inhibitors of hepatitis C virus. Campbell, Jeffrey Allen; Good, Andrew Charles (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003053349 A2 20030703, 225 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Haimos, Teddy; Linas-brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). PCT Int. Appl. WO 2000059929 A1 20001012, 154 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,

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R21

I

AB Macro cyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μ M in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN 2003:511084 Document No. 139:69527 Preparation of macrocyclic compounds as inhibitors of hepatitis C virus. Campbell, Jeffrey Allen; Good, Andrew Charles (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003053349 A2 20030703, 225 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Haimos, Teddy; Linas-brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). PCT Int. Appl. WO 2000059929 A1 20001012, 154 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,

TT, TZ, UU, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-CA353 20000403. PRIORITY: US 1999-PV128011 19990406. GI

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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

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L10 15 L1
=> 110 and crystal
1117482 CRYSTAL
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L14 ANSWER 1 OF 3 HCPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:252197 HCPLUS Full-text
DOCUMENT NUMBER: 140:281350
TITLE: Spiro compounds for inhibiting the first-pass effect
INVENTOR(S): Harris, James W.
PATENT ASSIGNEE(S): Bioavailability System, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S.
Ser. No. 793,416.
DOCUMENT TYPE: CODEN: USXXCO
Patent

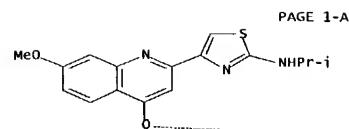
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| 19970826 | | | US 1997-997259 A2 |
| 19971223 | | | |
| OTHER SOURCE(S): | MARPAT | 140:281350 | |
| L14 ANSWER 2 OF 3 HCPLUS COPYRIGHT 2004 ACS on STN ACCESSION NUMBER: 2003:886572 HCPLUS Full-text DOCUMENT NUMBER: 140:122161 TITLE: An NS3 protease inhibitor with antiviral effects in humans infected with hepatitis C virus | | | |
| AUTHOR(S): Lamarre, Daniel; Anderson, Paul C.; Bailey, Murray; Pierre; Mireille; Goudreau, Lagace, Poupart, E.; St, Gerhard; Weldon, Steven | | | |
| CORPORATE SOURCE: Boehringer Ingelheim (Canada) Ltd, Laval, QC, H7S 2G5, Canada | | | |
| SOURCE: Nature (London, United Kingdom) (2003), 426(6963), 186-189 | | | |
| PUBLISHER: Nature Publishing Group | | | |

DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES
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L14 ANSWER 3 OF 3 HCPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:725652 HCPLUS Full-text
DOCUMENT NUMBER: 133:296659
TITLE: Preparation of macrocyclic peptides active against the hepatitis C virus
INVENTOR(S): Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Nathalie; Halmos, Anne-Marie; Ghiro, Elise; Goudreau, Teddy; Llinas-brunet, Montse Boehringer Ingelheim (Canada) Ltd., Can.
PATENT ASSIGNEE(S): PCT Int. Appl., 154 pp.
SOURCE: CODEN: PIXX02
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

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 20011004 <-- NO 2001004857 A 20011031 NO 2001-4857
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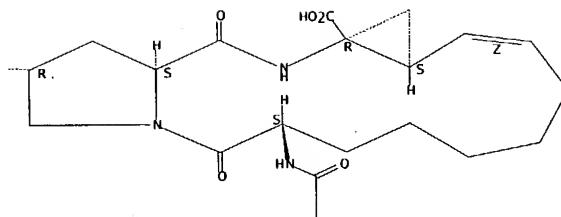


20000403 OTHER SOURCE(S): MARPAT 133:296659
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L14 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
 IT 300832-84-2, BILN 2061
 RL: THU (therapeutic use); BIOL (Biological study); USES (Uses)
 (spiro compds. for inhibiting the first-pass effect)
 RN 300832-84-2 HCAPLUS
 CN Cyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a(5H)-
 carboxylic acid, 6-[(cyclopentyloxy)carbonyl]amino-
 1,2,3,6,7,8,9,10,11,13a,14,15,16
 ,16a-tetradecahydro-2-[7-methoxy-2-[2-(1-methylethyl)amino]-4-
 thiazolinyl]-
 4-quinolinyl]oxy]-5,16-dioxo-, (2R,6S,12Z,13aS,14aR,16aS)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



PAGE 2-B

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 TOTAL
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 FULL ESTIMATED COST
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SINCE FILE
 ENTRY
 33.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
TOTAL ENTRY

SESSION CA SUBSCRIBER PRICE
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 TOTAL

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93.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
TOTAL ENTRY

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4.90

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 AGRICOLA,
 ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
 BABS,
 BIBLIODATA, BIOPARTNERS, BIOPARTNERS, BIOENGINEERING, BIOSIS,
 BIOTECHABS,
 BIOTECHOS, BIOTECHNO, BLDB, CABA, CANCERLIT, ...'
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EMBASE
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BIOSTS
INVESTEXT
MEDLINE
PCTFULL
CAPLUS
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DRUGU
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LIFESCI
PASCAL
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NLDB
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IFIPAT
PROMT

=> index f1-f29
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FULL ESTIMATED COST
94.22
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
TOTAL
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CA SUBSCRIBER PRICE
4.90
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ON 26 OCT 2004

29 FILES IN THE FILE LIST IN STNINDEX

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BIOTECHABS,
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15:24:55 ON
26 OCT 2004

SEA BILN 2061

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L15 QUE BILN 2061

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WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
2004

=> l15 and crystal?

FILE 'EMBASE'
48 "BILN"
124 "2061"
42 BILN 2061
("BILN"(W)"2061")
97097 CRYSTAL?
4 L15 AND CRYSTAL?

FILE 'SCISEARCH'
27 BILN
168 2061
22 BILN 2061
(BILN(W)2061)
689047 CRYSTAL?
3 L15 AND CRYSTAL?

FILE 'BIOSIS'
27 BILN
129 2061
18 BILN 2061
(BILN(W)2061)
111782 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'INVESTTEXT'

6 L15 AND CRYSTAL?
FILE 'LIFESCI'
5 "BILN"
28 "2061"
4 BILN 2061
("BILN"(W)"2061")
27296 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'PASCAL'
13 BILN
69 2061
4 BILN 2061
(BILN(W)2061)
517682 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'TOXCENTER'
6 BILN
63 2061
4 BILN 2061
(BILN(W)2061)
66181 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'ESBIOBASE'
3 BILN
49 2061
3 BILN 2061
(BILN(W)2061)
41699 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'IMSDRUGNEWS'
3 "BILN"
5 "2061"
3 BILN 2061
("BILN"(W)"2061")
118 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'NLDB'
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274 "2061"
3 BILN 2061
("BILN"(W)"2061")
32830 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'ADISCTI'
3 BILN
21 2061
2 BILN 2061
(BILN(W)2061)
463 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'BIOENG'
2 BILN
7 2061
2 BILN 2061
(BILN(W)2061)
7912 CRYSTAL?
0 L15 AND CRYSTAL?

20 "BILN"
1 "BILNS"
21 "BILN"
("BILN" OR "BILNS")
1864 "2061"
15 BILN 2061
("BILN"(W)"2061")
34452 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'MEDLINE'
19 BILN
122 2061
13 BILN 2061
(BILN(W)2061)
122732 CRYSTAL?
0 L15 AND CRYSTAL?
FILE 'PCTFULL'
40 BILN
2832 2061
11 BILN 2061
(BILN(W)2061)
127299 CRYSTAL?
9 L15 AND CRYSTAL?

FILE 'CAPLUS'
20 BILN
382 2061
10 BILN 2061
(BILN(W)2061)
1605797 CRYSTAL?
0 L15 AND CRYSTAL?
FILE 'DDFU'
13 BILN
21 2061
10 BILN 2061
(BILN(W)2061)
7961 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'DRUGU'
13 BILN
36 2061
10 BILN 2061
(BILN(W)2061)
12117 CRYSTAL?
0 L15 AND CRYSTAL?

FILE 'BIOTECHNO'
12 BILN
43 2061
8 BILN 2061
(BILN(W)2061)
27086 CRYSTAL?
3 L15 AND CRYSTAL?

FILE 'USPATFULL'
17 BILN
4661 2061
6 BILN 2061
(BILN(W)2061)
570101 CRYSTAL?

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FILE 'CBNB'
  2 BILN
  15 2061
  2 BILN 2061
    (BILN(W)2061)
  5823 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'COMPENDEX'
  4 BILN
  22 2061
  2 BILN 2061
    (BILN(W)2061)
  443469 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'PHIN'
  3 "BILN"
  35 "2061"
  2 BILN 2061
    ("BILN"(W)"2061")
  1251 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'WPIDS'
  4 BILN
  70 2061
  2 BILN 2061
    (BILN(W)2061)
  362675 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'WPINDEX'
  4 BILN
  70 2061
  2 BILN 2061
    (BILN(W)2061)
  362675 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'BABBS'
  1 BILN
  24 2061
  1 BILN 2061
    (BILN(W)2061)
  91052 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'CIN'
  1 "BILN"
  12 "2061"
  1 BILN 2061
    ("BILN"(W)"2061")
  6321 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'EMBAL'
  1 BILN
  4 2061
  1 BILN 2061
    (BILN(W)2061)
  1192 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'IFIPAT'

=> l16      25 L16
L18      dup rem
ENTER L# LIST OR (END):l18
PROCESSING COMPLETED FOR L18
L19      21 DUP REM L18 (4 DUPLICATES REMOVED)

=> l19 and pd<20030327
  1 FILES SEARCHED...
  3 FILES SEARCHED...
L20      2 L19 AND PD<20030327

=> d 120 1-2 ibib hitstr abs kwic
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

The following are valid formats:
The default display format is BIB.

ABS ----- AB
ALL ----- AN, DN, TX, AU, CS, SO, PUT, CY, DT, FS, LA, SL, AB,
          CT, RN, CN, NP, CO, GEN
BIB ----- AN, DN, TI, AU, CS, SO, PUT, CY, DT, FS, LA, SL
CBIB ----- Compressed bibliographic data
DALL ----- ALL, delimited for post-processing
IABS ----- ABS, with a text label
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- CT, RN, CN, NP, CO, GEN
TRIAL ----- TI, CT, RN, CN, NP, CO, GEN
(SAM, TRI)
HIT ----- All fields containing hit terms
HITIND ----- IND
KWIC ----- All hit terms plus 20 words on either side
OCC ----- List of display fields containing hit terms
          and number of occurrences in each field

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields, enter the display field codes. For a list of display field codes, enter 'HELP DFIELDS' at an arrow prompt (>). Examples of formats include: 'BIB'; 'AB'; 'SO,ST'. You may specify the format fields in any order, and the information will be displayed in the same order as the format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be used with the DISPLAY ACC command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):iall
L20 ANSWER 1 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
          on STN

  1 BILN
  39 2061
  1 BILN 2061
    (BILN(W)2061)
  146324 CRYSTAL?
    0 L15 AND CRYSTAL?
FILE 'PROMT'
  7 "BILN"
  538 "2061"
  1 BILN 2061
    ("BILN"(W)"2061")
  95992 CRYSTAL?
    0 L15 AND CRYSTAL?

L16  QUE L15 AND CRYSTAL?
=> d rank
F1          9  PCTFULL
F2          6  USPATFULL
F3          4  EMBASE
F4          3  SCISEARCH
F5          3  BIOTECHNO

=> file f3-5,f1,f2
COST IN U.S. DOLLARS
TOTAL
SESSION
  FULL ESTIMATED COST
  95.93
  1.71
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
TOTAL
SESSION
  CA SUBSCRIBER PRICE
  4.90
  0.00
ENTRY
FILE 'EMBASE' ENTERED AT 15:27:48 ON 26 OCT 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.
FILE 'SCISEARCH' ENTERED AT 15:27:48 ON 26 OCT 2004
Copyright (c) 2004 The Thomson Corporation.
FILE 'BIOTECHNO' ENTERED AT 15:27:48 ON 26 OCT 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.
FILE 'PCTFULL' ENTERED AT 15:27:48 ON 26 OCT 2004
COPYRIGHT (C) 2004 Univentio
FILE 'USPATFULL' ENTERED AT 15:27:48 ON 26 OCT 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
=> l16, dup rem
L17      0 L16, DUP REM

```

```

=> l16      25 L16
L18      dup rem
ENTER L# LIST OR (END):l18
PROCESSING COMPLETED FOR L18
L19      21 DUP REM L18 (4 DUPLICATES REMOVED)

=> l19 and pd<20030327
  1 FILES SEARCHED...
  3 FILES SEARCHED...
L20      2 L19 AND PD<20030327

=> d 120 1-2 ibib hitstr abs kwic
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

```

The following are valid formats:

The default display format is BIB.

```

ABS ----- AB
ALL ----- AN, DN, TX, AU, CS, SO, PUT, CY, DT, FS, LA, SL, AB,
          CT, RN, CN, NP, CO, GEN
BIB ----- AN, DN, TI, AU, CS, SO, PUT, CY, DT, FS, LA, SL
CBIB ----- Compressed bibliographic data
DALL ----- ALL, delimited for post-processing
IABS ----- ABS, with a text label
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- CT, RN, CN, NP, CO, GEN
TRIAL ----- TI, CT, RN, CN, NP, CO, GEN
(SAM, TRI)
HIT ----- All fields containing hit terms
HITIND ----- IND
KWIC ----- All hit terms plus 20 words on either side
OCC ----- List of display fields containing hit terms
          and number of occurrences in each field

```

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields, enter the display field codes. For a list of display field codes, enter 'HELP DFIELDS' at an arrow prompt (>). Examples of formats include: 'BIB'; 'AB'; 'SO,ST'. You may specify the format fields in any order, and the information will be displayed in the same order as the format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be used with the DISPLAY ACC command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):iall

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 on STN

ACCESSION NUMBER: 2003468113 EMBASE Full-text
TITLE: Current therapy and new molecular approaches to
 antiviral treatment and prevention of hepatitis C.
AUTHOR: Hugle T.; Cerny A.
CORPORATE SOURCE: Dr. A. Cerny, Clinica Medica, Ospedale Civico,
 CH-6903 Lugano, Switzerland. andreas.cerny@bluewin.ch
SOURCE: Reviews in Medical Virology, (2003) 13/6
 (361-371).
Refs: 79
ISSN: 1052-9276 CODEN: RMVIEW
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: Current therapeutic options for hepatitis C are limited, especially for
 genotype 1. For genotypes 2 and 3, pegylated interferon in
 combination with
 ribavirin, can lead to a sustained virological response in up to 80%
 of
 patients. Unfortunately, adverse effects of IFN and ribavirin are a
 major
 problem and the list of contraindications for HCV therapy is long,
 including
 decompensated cirrhosis of the liver and psychiatric disorders.
 Therefore,
 alternative therapeutic approaches are needed. New delivery options
 for IFN and
 ribavirin are aimed at optimising efficiency and reducing adverse
 effects.
 Recent progress in the molecular virology of HCV has identified new
 targets for
 antiviral intervention. Inhibition of HCV gene expression and
 replication as
 well as immunotherapeutic concepts aimed at enhancing the cellular
 immune
 response against HCV are being explored. Solution of the crystal
 structures of HCV key enzymes led to the design of specific
 inhibitors
 including compounds active against the well characterised NS3 serine
 protease
 and RNA-dependent RNA polymerase which are currently in the early
 phase
 clinical investigation. New strategies for inhibiting HCV gene
 expression
 include the use of antisense oligodeoxynucleotides and ribozymes.
 Immunomodulation by agents such as inosine monophosphate
 dehydrogenase
 inhibitors, thymosin-alpha 1, histamine or amantadine are being

studied in combination with IFN and/or ribavirin. Immunotherapeutic vaccination with recombinant HCV E1 protein improved host immunity against HCV and thus seems to be a promising new option. Copyright .COPYRGT. 2003 John Wiley & Sons, Ltd.

CONTROLLED TERM:

Medical Descriptors:
*hepatitis C: DT, drug therapy
*hepatitis C: ET, etiology
*hepatitis C: PC, prevention
*infection prevention
virus, gene
genotype
drug response
drug contraindication
drug delivery system
side effect: SI, side effect
gene expression
drug targeting
immunotherapy
enzyme structure
crystal structure
drug design
drug activity
antiviral activity
protein targeting
immunomodulation
vaccination
Hepatitis C virus
immune response
cellular immunity
hemolytic anemia: SI, side effect
mental disease: SI, side effect
flu like syndrome: SI, side effect
leukopenia: SI, side effect
thrombocytopenia: SI, side effect
teratogenicity
virus replication
drug hypersensitivity: SI, side effect
rash: SI, side effect
human
nonhuman
clinical trial
review
Drug Descriptors:
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: DT, drug therapy
alpha interferon: TO, drug toxicity
alpha interferon: PR, pharmacology
alpha interferon: PD, pharmacology
alpha interferon: SC, subcutaneous drug

administration

ribavirin: AE, adverse drug reaction

trial

ribozyme: CT, clinical trial
ribozyme: DT, drug therapy
ribozyme: TO, drug toxicity
ribozyme: PD, pharmacology
hepatozyme: AE, adverse drug reaction
hepatozyme: CT, clinical trial
hepatozyme: DT, drug therapy
hepatozyme: TO, drug toxicity
hepatozyme: PD, pharmacology
antisense oligodeoxynucleotide: CT, clinical trial
antisense oligodeoxynucleotide: DT, drug therapy
antisense oligodeoxynucleotide: PD, pharmacology
isis 14803: CT, clinical trial
isis 14803: DT, drug therapy
isis 14803: PD, pharmacology
RNA derivative: DV, drug development
RNA derivative: DT, drug therapy
RNA derivative: PD, pharmacology
small interfering rna: DV, drug development
small interfering rna: DT, drug therapy
small interfering rna: PD, pharmacology
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
xtl 002: DT, drug therapy
xtl 002: PD, pharmacology
cicavir: DT, drug therapy
cicavir: PD, pharmacology
immunomodulating agent: CB, drug combination
immunomodulating agent: DT, drug therapy
thymosin alpha1: CT, clinical trial
thymosin alpha1: CB, drug combination
thymosin alpha1: DO, drug dose
thymosin alpha1: DT, drug therapy
thymosin alpha1: PD, pharmacology
inosinate dehydrogenase inhibitor: CB, drug

combination therapy pharmacology

inosinate dehydrogenase inhibitor: DT, drug
inosinate dehydrogenase inhibitor: PD,
merimepodib: CT, clinical trial
merimepodib: CB, drug combination
merimepodib: DT, drug therapy
merimepodib: PD, pharmacology
unindexed drug
unclassified drug

CAS REGISTRY NO.: 37205-61-1;
198821-22-6,
CHEMICAL NAME: 198821-38-4
(1) Vx 950; (2) Jtk 003; Biln 2061; Isis 14803;
Xtl 002
(1) Vertex; (2) Akros; Ribozyme Pharmaceuticals;
NABI;
Scicline; RegeneRx; Maxim

ribavirin: CT, clinical trial
ribavirin: CB, drug combination
ribavirin: CM, drug comparison
ribavirin: DT, drug therapy
ribavirin: PK, pharmacokinetics
ribavirin: PD, pharmacology
ribavirin: PO, oral drug administration
albumin conjugate: PR, pharmacetics
liposome: PR, pharmacetics
polyaminoacid: PR, pharmacetics
polyaminoacid: PO, oral drug administration
ribavirin derivative: AE, adverse drug reaction
ribavirin derivative: CT, clinical trial
ribavirin derivative: CB, drug combination
ribavirin derivative: CM, drug comparison
ribavirin derivative: DT, drug therapy
ribavirin derivative: PD, pharmacology
viramidine: AE, adverse drug reaction
viramidine: CT, clinical trial
viramidine: CB, drug combination
viramidine: CM, drug comparison
viramidine: DT, drug therapy
viramidine: PD, pharmacology
levovirin: AE, adverse drug reaction
levovirin: CT, clinical trial
levovirin: CM, drug comparison
levovirin: DT, drug therapy
levovirin: PD, pharmacology
proteinase inhibitor: AE, adverse drug reaction
proteinase inhibitor: CT, clinical trial
proteinase inhibitor: DO, drug dose
proteinase inhibitor: DT, drug therapy
proteinase inhibitor: PK, pharmacokinetics
proteinase inhibitor: PD, pharmacology
proteinase inhibitor: PO, oral drug

administration

biln 2061: AE, adverse drug reaction
biln 2061: CT, clinical trial
biln 2061: DO, drug dose
biln 2061: DT, drug therapy
biln 2061: PK, pharmacokinetics
biln 2061: PD, pharmacology
biln 2061: PO, oral drug administration
vx 950: DT, drug therapy
vx 950: PD, pharmacology
virus, protein
protein NS5B
RNA directed DNA polymerase inhibitor: CT,
RNA directed DNA polymerase inhibitor: DT, drug
RNA directed DNA polymerase inhibitor: PD,
jtk 003: CT, clinical trial
jtk 003: DT, drug therapy
jtk 003: PD, pharmacology
ribozyme: AE, adverse drug reaction

clinical trial

therapy

pharmacology

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on STN
ACCESSION NUMBER: 2003195244 EMBASE Full-text
TITLE: Hepatitis C virus therapies: Current treatments, targets
AUTHOR: Hong Z.
CORPORATE SOURCE: Z. Hong, Ribapharm Inc., Hyland Avenue, Costa Mesa, CA,
SOURCE: United States. zhihong@ribapharm.com
Antiviral Chemistry and Chemotherapy, (2003) 14/1 (1-21).
Refs: 208
ISSN: 0956-3202 CODEN: ACCHEH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: Chronic hepatitis C virus (HCV) infection is the cause of an emerging global epidemic of chronic liver disease. Current combination therapies are at best 80% efficacious and are often poorly tolerated. Strategies to improve the therapeutic response include the development of novel interferons, nucleoside analogues with reduced haemolysis compared with ribavirin and inosine 5'-monophosphate dehydrogenase inhibitors. Compounds in preclinical or early clinical trials include small molecules that inhibit virus-specific enzymes (such as the serine proteases, RNA polymerase and helicase) or interfere with translation (including antisense molecules, tRNA and ribozymes). Advances in understanding HCV replication, obtaining a sub-genomic replicon and contriving potential small animal models, in addition to solving crystallographic structures for the replication enzymes, have improved prospects for developing novel therapies. This review summarizes current and evolving treatments for chronic hepatitis C infection. In addition, progress in HCV targets and drug discovery tools valuable in the search for novel anti-HCV agents is detailed.

| | | |
|-----------------|---|---|
| CONTROLED TERM: | Medical Descriptors: *hepatitis C: DT, drug therapy *hepatitis C: EP, epidemiology *hepatitis C: ET, etiology *chronic liver disease: ET, etiology drug efficacy drug tolerance hemolytic anemia: SI, side effect side effect: SI, side effect alanine aminotransferase blood level virus replication replicon crystal structure RNA translation untranslated region internal ribosome entry site monotherapy virus load treatment outcome treatment indication immunomodulation drug safety treatment failure chimpanzee transgenic mouse Hepatitis GB virus B IC 50 structure activity relation drug structure virus assembly human nonhuman clinical trial review priority journal Drug Descriptors: *antivirus agent: AE, adverse drug reaction *antivirus agent: CT, clinical trial *antivirus agent: AN, drug analysis *antivirus agent: CB, drug combination *antivirus agent: CM, drug comparison *antivirus agent: DV, drug development *antivirus agent: DO, drug dose *antivirus agent: DT, drug therapy *antivirus agent: PD, pharmacology *antivirus agent: IV, intravenous drug *antivirus agent: SC, subcutaneous drug alpha interferon: AE, adverse drug reaction alpha interferon: CB, drug combination alpha interferon: CM, drug comparison alpha interferon: DO, drug dose alpha interferon: DT, drug therapy alpha interferon: PD, pharmacology nucleoside derivative: AN, drug analysis nucleoside derivative: CM, drug comparison | nucleoside derivative: DV, drug development nucleoside derivative: PK, pharmaceutics nucleoside derivative: PD, pharmacology ribavirin: AE, adverse drug reaction ribavirin: CT, clinical trial ribavirin: CB, drug combination ribavirin: CM, drug comparison ribavirin: DO, drug dose ribavirin: DT, drug therapy ribavirin: PD, pharmacology inosinate dehydrogenase inhibitor: CM, drug inosinate dehydrogenase inhibitor: DT, drug inosinate dehydrogenase inhibitor: PD, serine proteinase: EC, endogenous compound RNA polymerase: EC, endogenous compound helicase: EC, endogenous compound ribozyme: EC, endogenous compound recombinant alpha ₂ interferon: CM, drug recombinant alpha ₂ interferon: DO, drug dose recombinant alpha ₂ interferon: DT, drug therapy recombinant alpha ₂ interferon: PD, pharmacology recombinant alpha ₂ interferon: SC, subcutaneous comparison therapy pharmacology |
| administration | | comparison comparison drug drug administration |
| administration | | administration consensus interferon: CM, drug comparison consensus interferon: DO, drug dose consensus interferon: DT, drug therapy consensus interferon: PD, pharmacology consensus interferon: SC, subcutaneous drug |
| administration | | peginterferon alpha _{2b} : CT, clinical trial peginterferon alpha _{2b} : CB, drug combination peginterferon alpha _{2b} : CM, drug comparison peginterferon alpha _{2b} : DO, drug dose peginterferon alpha _{2b} : DT, drug therapy peginterferon alpha _{2b} : PD, pharmacology peginterferon alpha _{2a} : CT, clinical trial peginterferon alpha _{2a} : CB, drug combination peginterferon alpha _{2a} : CM, drug comparison peginterferon alpha _{2a} : DO, drug dose peginterferon alpha _{2a} : DT, drug therapy peginterferon alpha _{2a} : PD, pharmacology levovirin: CT, clinical trial levovirin: AN, drug analysis levovirin: CM, drug comparison |
| administration | levovirin: DV, drug development levovirin: DO, drug dose levovirin: DT, drug therapy levovirin: PD, pharmacology viramidine: CT, clinical trial viramidine: AN, drug analysis viramidine: CM, drug comparison viramidine: DV, drug development viramidine: DO, drug dose viramidine: DT, drug therapy viramidine: PD, pharmacology merimepodib: CT, clinical trial merimepodib: AN, drug analysis merimepodib: CB, drug combination merimepodib: CM, drug comparison merimepodib: DV, drug development merimepodib: DT, drug therapy merimepodib: PD, pharmacology thymosin alpha ₁ : CT, clinical trial thymosin alpha ₁ : AN, drug analysis thymosin alpha ₁ : CB, drug combination thymosin alpha ₁ : DV, drug development thymosin alpha ₁ : DO, drug dose thymosin alpha ₁ : DT, drug therapy thymosin alpha ₁ : PD, pharmacology thymosin alpha ₁ : SC, subcutaneous drug amantadine: CT, clinical trial amantadine: AN, drug analysis amantadine: CB, drug combination amantadine: CM, drug comparison amantadine: DV, drug development amantadine: PD, pharmacology recombinant interleukin 12: CT, clinical trial recombinant interleukin 12: AN, drug analysis recombinant interleukin 12: CB, drug combination recombinant interleukin 12: CM, drug comparison recombinant interleukin 12: DV, drug development recombinant interleukin 12: DO, drug dose recombinant interleukin 12: DT, drug therapy recombinant interleukin 12: PD, pharmacology histamine: CT, clinical trial histamine: AN, drug analysis histamine: CB, drug combination histamine: DV, drug development histamine: DT, drug therapy histamine: PD, pharmacology gamma interferon: CT, clinical trial gamma interferon: AN, drug analysis gamma interferon: CB, drug combination gamma interferon: DV, drug development gamma interferon: DT, drug therapy gamma interferon: PD, pharmacology proteinase inhibitor: CT, clinical trial proteinase inhibitor: DO, drug dose proteinase inhibitor: PD, pharmacology proteinase inhibitor: PO, oral drug | administration peptide derivative: AN, drug analysis peptide derivative: DV, drug development peptide derivative: PD, pharmacology peptide alpha keto acid: AN, drug analysis peptide alpha keto acid: DV, drug development peptide alpha keto acid: PD, pharmacology pyrrolidine derivative: AN, drug analysis pyrrolidine derivative: DV, drug development pyrrolidine derivative: PD, pharmacology pyrrolidine 5,5 lactam: AN, drug analysis pyrrolidine 5,5 lactam: DV, drug development pyrrolidine 5,5 lactam: PD, pharmacology IDdb3: DV, drug development IDdb3: PD, pharmacology unindexed drug unclassified drug isis 14803 gw 3112 gw 2549 gw 0569 n [4 [[[6,7 dihydro 2 (4 methylphenyl) 5h 8 yl]carbonyl]amino]benzyl] n,n dimethyl 2h 4 aminium chloride 1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane) (ribavirin) 36791-04-5; (serine proteinase) (RNA polymerase) 9014-24-8; (helicase) 42613-29- (recombinant alpha _{2b} interferon) 98530-12-2; alpha _{2b}) 215647-85-1; (peginterferon alpha _{2a}) (merimepodib) 198821-22-6, 198821-38-4; (thymosin 69521-94-4; (amantadine) 665-66-7, 768-94-5; 51-45-6, 56-92-8, 93443-21-1; (gamma interferon) 82115-62-6; (proteinase inhibitor) 37205-61-1; (n dihydro 2 (4 methylphenyl) 5h benzocyclohepten 8 yl]carbonyl]amino]benzyl] n, dimethyl 2h aminium chloride) 229005-80-5; (1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane)) 155148-31-5 (1) Vx 497; (2) Ceplene; (3) Biln 2061; (4) Isis 14803; Zadaxin; Gw 3112; Gw 2549; Gw 0569; Tak 3100; IDdb3 |
| administration | CAS REGISTRY NO.: 37259-58-8; 6; (peginterferon 198153-51-4; alpha1) (histamine) [4 [[[6,7 tetrahydropyran 4 CHEMICAL NAME: 779; Amd | administration benzocyclohepten tetrahydropyran CAS REGISTRY NO.: 37259-58-8; 6; (peginterferon 198153-51-4; alpha1) (histamine) [4 [[[6,7 tetrahydropyran 4 CHEMICAL NAME: 779; Amd |

COMPANY NAME: (1) Vertex (United States); (2) Maxim; (3) Boehringer Ingelheim; (4) Isis (United States); Ribapharm; Merck (United States); Glaxo SmithKline (United Kingdom); Bristol Myers Squibb (United States); Celera (United States); Viropharma; Japanese tobacco; IRBM

=> d his

(FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPUP, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON 26 OCT 2004

FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
L1 1 S 300832-84-2/RN

SET SMA OFF
DEL SEL Y
SEL RN
SET SMA LOGIN

INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
SEA E1 AND OPTICAL?/FA

L2 QUE 300832-84-2/B1 AND OPTICAL?/FA

FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
L3 0 S L1/BMF

FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
L4 0 S L1/BPN

FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
L5 0 S L1/IMF

FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
L6 1 S L1/PEP

FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT. 2004
L7 0 S L1/PUR

FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
L8 6 S (L1/SPN OR L1/CPN)
L9 6 FOCUS L8 1-

FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

IMS DRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN, WPIOS, WPINDEX, BABS, CTN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON 26 OCT 2004

SEA L15 AND CRYSTAL?
4 FILE EMBASE
3 FILE SCISEARCH
9 FILE PCTFULL
3 FILE BIOTECHNO
6 FILE USPATFULL
QUE L15 AND CRYSTAL?

FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED AT 15:27:48 ON 26 OCT 2004
L17 0 L16, DUP REM
L18 25 L16
L19 21 DUP REM L18 (4 DUPLICATES REMOVED)
L20 2 L19 AND PD<20030327

=> STNINDEX
ENTER FILE OR CLUSTER NAMES (NONE):all
FILE 'ENCOMPLIT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPLIT2' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT2' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS

TOTAL SINCE FILE
SESSION ENTRY
SESSION FULL ESTIMATED COST 16.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL ENTRY

SESSION CA SUBSCRIBER PRICE 0.00 -
4.90

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA, ALUMINUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS, BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, BLLOB, CABA, CANCERLIT, ...' ENTERED AT 15:32:46 ON 26 OCT 2004

143 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view search error messages that display as 0" with SET DETAIL OFF.

FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004
L10 15 S L1
L11 0 L10 AND CRYSTAL
L12 0 L10 AND CRYSTAL?
L13 0 L10 AND ALCOHOL
L14 3 L10 AND PD<20030327

FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA, ALUMINUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS, BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, BLLOB, CABA, CANCERLIT, ...' ENTERED AT 15:24:55 ON 26 OCT 2004

SEA BILN 2061

2 FILE ADISCTI
1 FILE BABS
2 FILE BIOENG
18 FILE BIOSIS
8 FILE BIOTECHNO
10 FILE CAPLUS
2 FILE CBNB
1 FILE CIN
2 FILE COMPENDEX
10 FILE DDFU
10 FILE DRUGU
1 FILE EMBAL
42 FILE EMBASE
3 FILE ESBIOSA
1 FILE IFIPAT
3 FILE IMSDRUGNEWS
15 FILE INVESTTEXT
4 FILE LIFESCI
13 FILE MEDLINE
3 FILE NLDB
4 FILE PASCAL
11 FILE PCTFULL
2 FILE PHIN
1 FILE PROMT
22 FILE SCISEARCH
4 FILE TOXCENTER
6 FILE USPATFULL
2 FILE WPIDS
2 FILE WPINDEX
L15 QUE BILN 2061

INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTTEXT, MEDLINE, PCTFULL, CAPLUS, DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER, ESBIOSA',

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FILE 'ABI-INFORM'
'CN' IS NOT A VALID FIELD CODE
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FILE 'AEROSPACE'
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FILE 'ANABSTR'
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FILE 'APOLLIT'
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'CN' IS NOT A VALID FIELD CODE
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FILE 'BABS'
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FILE 'BIBLIODATA'
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FILE 'BIOBUSINESS'
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FILE 'BIOCOMMERCE'
'CN' IS NOT A VALID FIELD CODE
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<----User Break---->
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FILE 'BIOSIS'
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SEARCH ENDED BY USER
FILE 'BIOTECHABS'
SEARCH ENDED BY USER

=> ciluprevir/
FILE 'IMOBILITY'
'CILUPREVIR/' IS NOT A VALID FIELD CODE
For a list of field codes for the current file, enter "HELP SFIELDS"
at an arrow prompt (=>).

=> ciluprevir
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FILE '2MOBILITY'
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FILE 'ABI-INFORM'
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FILE 'CIN' 0 CILUPREVIR
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FILE 'CIVILENG' 0 CILUPREVIR

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FILE 'EMA'

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FILE 'EMBASE' 3 CILUPREVIR
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FILE 'ENVIROENG' 0 CILUPREVIR
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FILE 'EUROPATFULL' 0 CILUPREVIR
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FILE 'FOMAD' 0 CILUPREVIR
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FILE 'FORIS' 0 CILUPREVIR
FILE 'FRANCEPAT' 0 CILUPREVIR
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FILE 'FRFULL' 0 CILUPREVIR
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FILE 'FROSTI' 0 CILUPREVIR
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FILE 'IFIPAT' 0 CILUPREVIR
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FILE 'IMSDRUGNEWS' 0 CILUPREVIR

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FILE 'WTEXTILES' 0 CILUPREVIR
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L21 QUE CILUPREVIR
=> d rank
F1 3 EMBASE
F2 2 ESBIOBASE
F3 2 MEDLINE
F4 2 SCISEARCH
F5 1 DDFU
F6 1 DRUGU

=> fil f1-6
COST IN U.S. DOLLARS SINCE FILE
TOTAL ENTRY

SESSION
FULL ESTIMATED COST 5.70
118.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL ENTRY

SESSION
CA SUBSCRIBER PRICE 0.00
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FILE 'MEDLINE' ENTERED AT 15:39:01 ON 26 OCT 2004

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FILE 'DDFU' ACCESS NOT AUTHORIZED

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=> s 121
L22 10 L21

=> L22 and pd<20030327
1 FILES SEARCHED..
2 FILES SEARCHED.
'20030327' NOT A VALID FIELD CODE
'20030327' NOT A VALID FIELD CODE
L23 1 L22 AND PD<20030327

=> d 123

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on STN
AN 2004039472 EMBASE Full-text
TI Gateways to Clinical Trials.
AU Bayes M.; Rabasseda X.; Prous J.R.
CS M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain.
mbayes@prous.com
SO Methods and Findings in Experimental and Clinical Pharmacology,
(2003) 25/10 (831-855).
Refs: 145
ISSN: 0379-0355 CODEN: MFEPDX
CY Spain
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English

=> FIL STNGUIDE
COST IN U.S. DOLLARS
TOTAL

SINCE FILE

ENTRY

SESSION
FULL ESTIMATED COST
126.52

8.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

ENTRY

SESSION
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4.90

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 22, 2004 (20041022/UP).

=> l23 all

MISSING OPERATOR L23 ALL
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d 123 all

YOU HAVE REQUESTED DATA FROM FILE 'EMBASE' - CONTINUE? (Y)/N:y

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on STN
AN 2004039472 EMBASE Full-text
TI Gateways to Clinical Trials.
AU Bayes M.; Rabasseda X.; Prous J.R.
CS M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain.
mbayes@prous.com
SO Methods and Findings in Experimental and Clinical Pharmacology,
(2003) 25/10 (831-855).
Refs: 145
ISSN: 0379-0355 CODEN: MFEPDX
CY Spain
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity®, the drug discovery and development portal, <http://integrity.prous.com>. This issue focuses on the following selection of drugs: Abetimus sodium, adalimumab, alefacent, alemtuzumab, almotriptan, AMGN-0007, anakinra, anti-CTLA-4 Mab, L-arginine hydrochloride, arzoxifene hydrochloride, astemizole, atazanavir sulfate, atizumab; Belimumab, BG-9928, binodenoson, bosentan, botulinum toxin type B, bovine lactoferrin, BufferGel, Caspofungin acetate, ciclesonide, cilomilast, ciluprevir, clofarabine, CTV-3146; Darbepoetin alfa, desloratadine, diflomotecan, doripenem, dronedarone hydrochloride, drotrecogin alfa (activated), DT388-GM-CSF, duloxetine hydrochloride, E-5564, efalizumab, enfuvirtide, esomeprazole magnesium, estradiol acetate, ETC-642,

efalizumab; CT, clinical trial
imatinib; CT, clinical trial
terfenadine; CT, clinical trial
Tipranavir; CT, clinical trial
Tipranavir; PO, oral drug administration
Ximelegatran; CT, clinical trial
Ximelegatran; PO, oral drug administration
YM 337; CT, clinical trial
moxidectin; CT, clinical trial
estradiol; CT, clinical trial
novel erythropoiesis stimulating protein; CT, clinical trial
novel erythropoiesis stimulating protein; IV, intravenous drug administration
novel erythropoiesis stimulating protein; SC, subcutaneous drug administration
desloratadine; CT, clinical trial
desloratadine; PO, oral drug administration
diflomotecan; CT, clinical trial
diflomotecan; IV, intravenous drug administration
diflomotecan; PO, oral drug administration
morphine; CT, clinical trial
etiracetam; CT, clinical trial
doripenem; CT, clinical trial
duloxetine; CT, clinical trial
unindex drug
RN (abetimus) 167362-48-3, 169147-32-4; (adalimumab) 331731-18-1;
(linezolid) 165800-03-3; (alemtuzumab) 216503-57-0; (ivabradine) 148849-67-6,
148870-80-8, 155974-00-8; (glucagon like peptide 1) 89750-14-1;
(astemizole) 68844-77-9; (atazanavir) 198904-31-3; (bosentan)
147536-97-8, 157212-55-0; (caspofungin) 189768-38-5; (ciclesonide) 126544-47-6;
(cilmilast) 153259-65-5; (efalizumab) 214745-43-4; (imatinib) 152459-95-5, 220127-57-1; (terfenadine) 50679-08-8; (tipranavir) 174484-41-4; (ximelegatran) 192939-46-1, 260790-58-7;
(moxidectin) 113507-06-5; (estradiol) 50-28-2; (desloratadine) 100643-71-8;
(diflomotecan) 220997-97-7; (morphine) 52-26-6, 57-27-2;
(etiracetam) 102767-28-2, 33996-58-6; (doripenem) 148016-81-3; (duloxetine) 116539-59-4, 136434-34-9
CN YM 337

=> DIS HIST

(FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

INDEX 'ADISCTI', 'ADISINSIGHT', 'ADISNEWS', 'AGRICOLA', 'ANABSTR', 'ANTE',
AQUALINE,
AQUASCII, 'BIOBUSINESS', 'BIOCOPMERC', 'BIOENG', 'BIOSIS', 'BIOTECHABS',
BIOTECNO, 'CABA', 'CANCERLIT', 'CAPLUS', 'CEABA-VTB', 'CEN', 'CIN',
CONFSCI, 'CROPB',
CROPU, 'DDFB', 'DDFU', 'DGEDE', 'DISSABS', ...' ENTERED AT 14:25:23 ON

exenatide, exisulind, ezetimib; Febuxostat; Gallium maltolate,
ganirelix acetate, garenoxacin mesilate, gefitinib; H11, HuMax;
IL-15, IDD-1, IGV-C, imatinib mesylate, ISIS-14803, ITF-1697,
ivabradine hydrochloride; KRN-5500; L-365260, Levetiracetam,
levosimendan, licofelone, linezolid, LJP-1082, lopinavir
lumiracoxib; MCC-478, melatonin, morphine hydrochloride,
morphine-6-glucuronide, moxidectin; N-Acetylcarnosine,
natalizumab, NM-702, NNC-05-1869, NSC-703940; Ocinafion OM-89,
omalizumab, omeprazole/sodium bicarbonate, OPC-28326,
osipemifene; PEG-filgrastim peginterferon alfa-2a, pegsunercept,
pirfenidone, pralmorelin, pregabalin; Recombinant glucagon-like
peptide 1 (7-36) amide, repifermin, RSD-1235; S-8184,
selodenoson, sodium dichloroacetate, suberanilohydroxamic acid;
TAS-102, terfenadine, teriparatide, tipranavir troxacitabine;
Ximelagatran; YM-337. ©PYRG. 2003 Prous Science. All rights reserved.
CT Medical Descriptors:
*drug monitoring
drug indication
drug efficacy
drug safety
side effect; SI, side effect
patient compliance
drug tolerability
liver toxicity; SI, side effect
bleeding; SI, side effect
disease exacerbation
systemic lupus erythematosus; SI, side effect
digestive system ulcer; SI, side effect
neutropenia; SI, side effect
teratogenicity; SI, side effect
human
clinical trial
review
Drug Descriptors:
abetimus; CT, clinical trial
abetimus; IV, intravenous drug administration
adalimumab; AE, adverse drug reaction
adalimumab; CT, clinical trial
linezolid; CT, clinical trial
alemtuzumab; CT, clinical trial
ivabradine; CT, clinical trial
ivabradine; IV, intravenous drug administration
recombinant interleukin 1 receptor blocking agent; CT, clinical trial
recombinant interleukin 1 receptor blocking agent; IA,
intraarterial drug
administration
glucagon like peptide 1; CT, clinical trial
glucagon like peptide 1; SC, subcutaneous drug administration
astemizole; CT, clinical trial
atazanavir; CT, clinical trial
bosentan; CT, clinical trial
botulinum toxin B; CT, clinical trial
caspofungin; CT, clinical trial
ciclesonide; CT, clinical trial
cilmilast; CT, clinical trial

26 OCT 2004

L1 FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004

1 S 300832-84-2/RN
SET SMA OFF
DEL SEL Y
SEL RN
SET SMA LOGIN

INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
SEA E1 AND OPTICAL?/FA

L2 QUE 300832-84-2/BI AND OPTICAL?/FA

FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
0 S L1/BMF

L4 FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
0 S L1/BPN

L5 FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
0 S L1/IMF

L6 FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
1 S L1/PEP

L7 FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
0 S L1/PUR

L8 FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
6 S (L1/SPN OR L1/CPN)
6 FOCUS L8 1-

FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004

L10 15 S L1
L11 0 L10 AND CRYSTAL
L12 0 L10 AND CRYSTAL?
L13 0 L10 AND ALCOHOL
L14 3 L10 AND PD<20030327

FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
BIBLIODATA, BIOPARTNERS, BIOMERCE, BIOENG, BIOSIS,
BIOTECHABS,
BIOTECHDS, BIOTECHNO, BLldb, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
26 OCT 2004
SEA BILN 2061

2 FILE ADISCTI

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
BIBLIODATA, BIOPARTNERS, BIOMERCE, BIOENG, BIOSIS,
BIOTECHABS,
BIOTECHDS, BIOTECHNO, BLldb, CABA, CANCERLIT, ...' ENTERED AT
15:32:46 ON
26 OCT 2004
SEA CILUPREVIR/CN

0* FILE 1MOBILITY
0* FILE 2MOBILITY
0* FILE ADISCTI
0* FILE AEROSPACE
0* FILE ALUMINIUM
0* FILE ANTE
0* FILE APOLLIT
0* FILE AQUALINE
0* FILE AQUASCI
0* FILE BABS
0* FILE BIBLIODATA
0* FILE BIOMERCE
0* FILE BIOENG
SEA CILUPREVIR/

0* FILE 1MOBILITY
SEA CILUPREVIR

1 FILE DDFU
1 FILE DRUGU
3 FILE EMBASE
2 FILE ESBIODEBASE
2 FILE MEDLINE
2 FILE SCISEARCH

L21 QUE CILUPREVIR

FILE 'EMBASE, ESBIODEBASE, MEDLINE, SCISEARCH, DRUGU' ENTERED AT
15:39:01
ON 26 OCT 2004
L22 10 S L21
L23 1 L22 AND PD<20030327

FILE 'STNGUIDE' ENTERED AT 15:40:30 ON 26 OCT 2004

FILE 'EMBASE' ENTERED AT 15:41:46 ON 26 OCT 2004

FILE 'STNGUIDE' ENTERED AT 15:41:46 ON 26 OCT 2004

=>

---Logging off of STN---

1 FILE BABS
2 FILE BIOENG
18 FILE BIOSIS
8 FILE BIOTECHNO
10 FILE CAPLUS
2 FILE CBNB
1 FILE CIN
2 FILE COMPENDEX
10 FILE DDFU
10 FILE DRUGU
1 FILE EMBAL
42 FILE EMBASE
3 FILE ESBIODEBASE
1 FILE IFIPAT
3 FILE IMSDRUGNEWS
15 FILE INVESTTEXT
4 FILE LIFESCI
13 FILE MEDLINE
3 FILE NLDB
4 FILE PASCAL
11 FILE PCTFULL
2 FILE PHIN
1 FILE PROMT
22 FILE SCISEARCH
4 FILE TOXCENTER
6 FILE USPATFULL
2 FILE WPIDS
2 FILE WPINDEX
L15 QUE BILN 2061

INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTTEXT, MEDLINE, PCTFULL,
CAPLUS,
DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIODEBASE,
IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
2004

SEA L15 AND CRYSTAL?

4 FILE EMBASE
3 FILE SCISEARCH
9 FILE PCTFULL
3 FILE BIOTECHNO
6 FILE USPATFULL

L16 QUE L15 AND CRYSTAL?

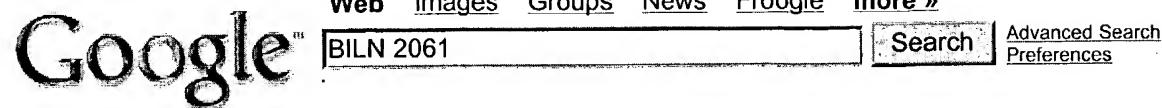
FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
AT 15:27:48 ON 26 OCT 2004
L17 0 L16, DUP REM
L18 25 L16
L19 21 DUP REM L18 (4 DUPLICATES REMOVED)
L20 2 L19 AND PD<20030327

=>
Executing the logoff script...

=> LOG Y

| COST IN U.S. DOLLARS | SINCE FILE |
|--|------------|
| TOTAL | ENTRY |
| SESSION | |
| FULL ESTIMATED COST | 0.12 |
| 130.58 | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE |
| TOTAL | ENTRY |
| SESSION | |
| CA SUBSCRIBER PRICE | 0.00 |
| 4.90 | |

STN INTERNATIONAL LOGOFF AT 15:42:43 ON 26 OCT 2004

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Inhibitor from Boehringer Ingelheim By Mark Nelson, MD. By Mark Nelson. ...

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Oct 27, 7:00 PM ET. Source: Acurian Inc. by: Darrin Kiessling. ...

dynamics.org/~altenber/cryo/HCV/BILN2061.Yahoo.html - 43k - [Cached](#) - [Similar pages](#)**Hepatitis C Vets, Orally available Hepatitis C Virus (HCV) ...**... Orally available Hepatitis C Virus (HCV) Protease Inhibitor (**BILN 2061**, Boehringer Ingelheim Pharma) Demonstrates Potent Anti-viral Activity in Persons ...hepcvets.com/drugs/biln2061.html - 11k - [Cached](#) - [Similar pages](#)**ISMC 2004: Session 2A: The discovery of BILN 2061, an NS3 protease ...**Session 2A: Keynote lecture. The discovery of **BILN 2061**, an NS3 protease inhibitor with antiviral effects in humans infected with hepatitis C virus. ...www.ismc2004.dk/index.php/Session_2A__The_discovery_of_B/258/0/ - 11k - [Cached](#) - [Similar pages](#)**54th Annual Meeting of**... **BILN 2061** Establishes Proof-of-Concept in Humans for an HCV Protease Inhibitor ... Note:**BILN 2061** is in clinical development by Boehringer Ingelheim. 10/29/03. ...janis7hepc.com/54th_annual_meeting_of10.htm - 101k - Oct 24, 2004 - [Cached](#) - [Similar pages](#)**Clinical Care Options for Hepatitis - BILN 2061 Inhibits HCV ...****BILN 2061** Inhibits HCV Genotype 2 and 3 Proteases in Vitro, ... This study examined the ability of **BILN 2061** to inhibit NS3 protease from genotypes 2 and 3. ...clinicaloptions.com/hep/conf/aasd2003/cs/300.asp - 20k - [Cached](#) - [Similar pages](#)**Clinical Care Options for Hepatitis - BILN 2061 shows promise in ...****BILN 2061** shows promise in early clinical trial against HCV genotype 1,Deanna M. Green, PhD. November 18, 2003 — **BILN 2061** induces ...clinicaloptions.com/hep/news/news_imed_2.asp - 20k - [Cached](#) - [Similar pages](#)[More results from clinicaloptions.com]**Serin-Protease-Hemmstoff (**BILN-2061**) bei Hepatitis-C - [Translate this page]**

... Medizinrecht. Neue Medikamente im Pipeline 2002. Serin-Protease-Hemmstoff

(BILN-2061) bei Hepatitis-C. ... Die Arbeiten zu **BILN 2061** befinden sich am Anfangsphase. ...www.medknowledge.de/neu/2002/IV-2002-32-biln-2061-pipeline.htm - 38k - [Cached](#) - [Similar pages](#)**HIV Report Jan 2003: A Promising New Anti-HCV Protease Inhibitor**... Researchers presented 4 papers describing the discovery, safety and early antiviral activity of **BILN 2061**, a serine protease inhibitor [Hepatology 2002;36:167A ...www.hopkins-aids.edu/publications/report/jan03_4.html - 11k - [Cached](#) - [Similar pages](#)

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Results 1 - 10 of about 20 for **ciluprevir**. (0.21 seconds)[\[doc\] N03](#)File Format: Microsoft Word 2000 - [View as HTML](#)... COUNCIL: USAN **CILUPREVIR**. PRONUNCIATION (si loo pre' veer). THERAPEUTIC CLAIM Treatment of Hepatitis C infection. CHEMICAL NAMES. 1 ...www.ama-assn.org/ama1/pub/upload/mm/365/ciluprevir.doc - [Similar pages](#)

AMA (USAN) 2004 Published USAN

... atilmotin avanafil becatecarin bemotrizinol bisotrizole canfosfamide hydrochloride cariporide mesylate ciclesonide **ciluprevir** dabuzalgron hydrochloride ...www.ama-assn.org/ama/pub/category/9615.html - 17k - [Cached](#) - [Similar pages](#)

Antiviral compounds; TerraQSAR-LOGP computed octanol/water ...

... ciclofoxolone, 52247-86-6, C38H56O7, 624.86, 4.15. **ciluprevir**, 300832-84-2, C40H50N6O8S, 774.94, -0.53. streptovarycin, 1404-74-6, C40H51NO14, 769.84, 1.87. ...www.terrabase-inc.com/antivirals.html - 11k - [Cached](#) - [Similar pages](#)

[Report] Global PharmaVitae Boehringer Ingelheim Market Research ...

... and forecast revenue growth Other products Marketed products R&D compounds Micardis (telmisartan) BIBH-1 (sibrotuzumab) BILN 2061(**ciluprevir**) BIBT 986 BIWI-1 ...www.the-infoshop.com/study/dc21221_boehringer_ingroup_toc.html - 28k - [Cached](#) - [Similar pages](#)

PharmaVitae 2004: Boehringer Ingelheim Global Analysis: Table of ...

... 94. R&D compounds. 95. Micardis (telmisartan). 96. BIBH-1 (sibrotuzumab). 96. BILN 2061(**ciluprevir**). 96. BIBT 986. 97. BIWI-1 (bivatuzumab mertansine). 97. ...www.datamonitor.com/~a36ec16c415a44bbaaf54fea6eee497e~/products/free/CompanyReport/CSHC1165/020cshc1165.htm - 27k - [Cached](#) - [Similar pages](#)

Gateways to clinical trials.

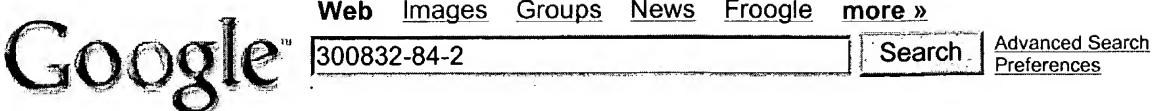
... BG-9928, binodenoson, bosentan, botulinum toxin type B, bovine lactoferrin, BufferGel; Caspofungin acetate, ciclesonide, cilomilast, **ciluprevir**, clofarabine, CVT ...www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14735233&dopt=Abstract - [Similar pages](#)

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... Bevacizumab, BG-9928, BMS-188667, botulinum toxin type B, BufferGel; Caffeine, CDP-870, cetuximab, cilomilast, **ciluprevir**, clofarabine, continuous ...www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list_uids=14988742 - [Similar pages](#)

Datamonitor Research Reports -- PharmaVitae 2004: Boehringer ...

... 96. R&D compounds. 97. Micardis (telmisartan). 98. BIBH-1 (sibrotuzumab). 98. BILN 2061(**ciluprevir**). 98. BIBT 986. 99. BIWI-1 (bivatuzumab mertansine). 99. ...www.datamonitorcp58.htm - 101k - [Cached](#) - [Similar pages](#)www.ciluprevir.net/[Similar pages](#)www.ciluprevir.com/[Similar pages](#)



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300 832 - 84 - 2 = 300 746

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Antiviral compounds; TerraQSAR-LOGP computed octanol/water ...

... cicloolone, 52247-86-6, C38H56O7, 624.86, 4.15. ciluprevir, **300832-84-2**, C40H50N6O8S, 774.94, -0.53. streptovarycin, 1404-74-6, C40H51NO14, 769.84, 1.87. ...

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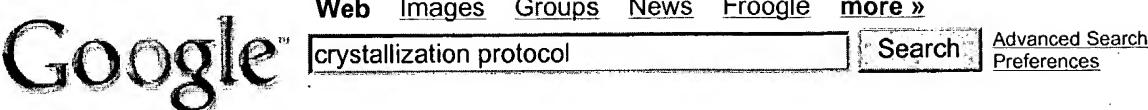
... TRADEMARK Unknown as yet. MANUFACTURER Boehringer Ingelheim Pharma GmbH & Co. KG.
CODE DESIGNATION BILN 2061 ZW. CAS REGISTRY NUMBER **300832-84-2**.

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... **Protocols**: A Practical Guide to Protein **Crystallization** (Mark Knapp and Bernhard Rupp) In order to obtain a **crystal**, the protein molecules must assemble into a ...

www.protocol-online.org/prot/Biochemistry_Amino_Acids_Protein/Protein_Crystallization/ - 9k - Cached - Similar pages

Definition of Category exptl_crystal_grow_comp

... However, the number of solutions required to describe the **crystallization protocol**

is not limited to 2. Details of the **crystallization protocol** should be ...

msdlocal.ebi.ac.uk/docs/exchange/mmcif_rcsb_nmr.dic/Categories/exptl_crystal_grow_comp.html - 8k - Cached - Similar pages

High Throughput Protein Crystallization

... with the aim to establish correlations between **crystallization** probability and ... Such an optimized **protocol** maximizes the probability of success while minimizing ...

www-structure.llnl.gov/Xray/tutorial/High_Throughput_EMBL_full.htm - 79k - Cached - Similar pages

CRYSTOOL Move announcement

CRYSTOOL. Has Moved. There is a new implementation of Brent Segelke's CRYSTOOL program

[1] for creating efficient, customizable, random **crystallization** screens. ...

www-structure.llnl.gov/crystool/crystool.htm - 3k - Cached - Similar pages

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(IUCr) Crystallization experiments with 2-enoyl-CoA hydratase ...

... Volume 50 Part 4 Pages 443-447 July 1994 **Crystallization** experiments with 2-enoyl-CoA hydratase, using an automated 'fast-screening' **crystallization protocol**. ...

scripts.iucr.org/cgi-bin/paper?gr0322 - Similar pages

Protein Crystal Structure Team I | RIKEN

... (2), Development of high-throughput protein **crystallization protocol** for large scale.

(3), Development of in situ X-ray diffractometer for protein **crystal**. image ...

www.riken.go.jp/engn/r-world/research/lab/harima/group-h/crystal1/ - 12k - Cached - Similar pages

Micro-seeding Procedure

... Pre-equilibrated drops contain protein and precipitant that is at a concentration just below what is required for precipitation or **crystallization** of the ...

www.hhmi.swmed.edu/Labs/rr/world/seeding.html - 3k - Cached - Similar pages

X-tal protocols: References.

... D50, 443-447 **Crystallization** Experiments with 2-Enoyl-CoA Hydratase, Using an Automated 'Fast-Screening' **Crystallization Protocol**. ...

www.xtal-protocols.de/ref/reference.html - 9k - Cached - Similar pages

Protein Crystallization

... Label your concentrated protein with a batch number. Differences in the purification **protocols** may later relate to irreproducibility in **crystallization**; ...

www-structmed.cimr.cam.ac.uk/Course/Crystals/Screening/hd_protocol.html - 4k - Cached - Similar pages

The Scientist :: Crystal Illumination, Jan. 19, 2004

... usually 50 nanoliters, is so crucial to its drug-discovery efforts that the company has patented its proprietary Nano- volume **Crystallization™ protocol**. ...

www.the-scientist.com/yr2004/jan/tech1_040119.html - Similar pages



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| #3 Search crystallization | 09:46:56 | 25455 |
| #2 Search hplc purification column heat | 09:07:15 | 123 |
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